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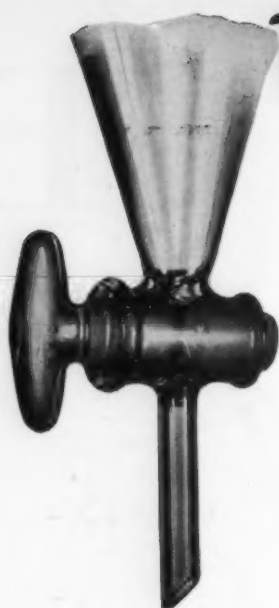
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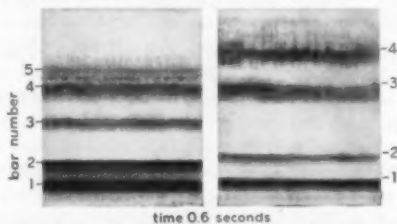
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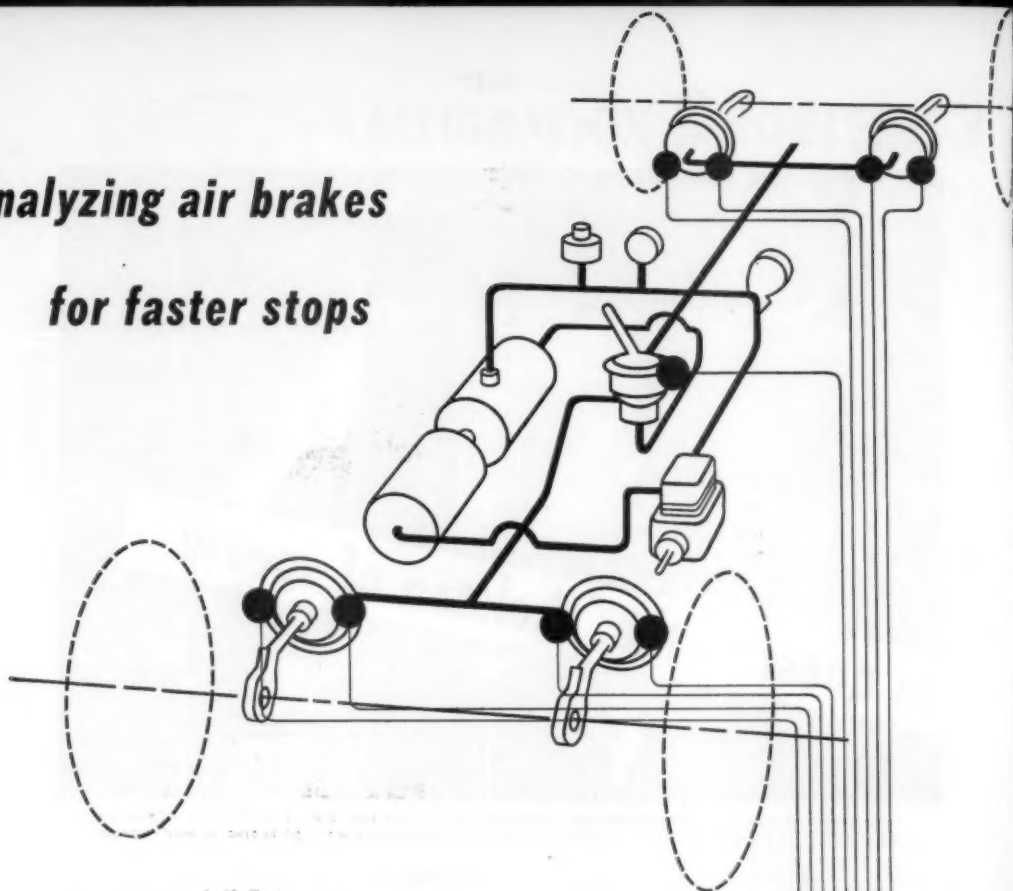
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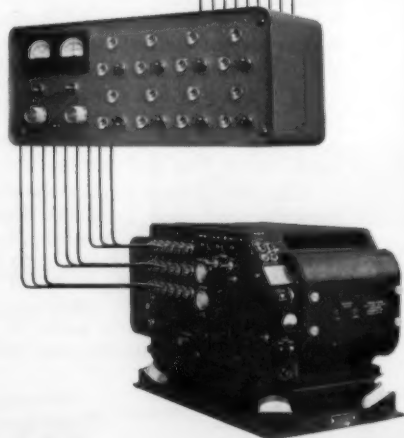
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The Agricultural Board was established under the NRC in 1944 upon joint recommendation of the Division of Biology and Agriculture and of the Association of Land-Grant Colleges and Universities. Although members serve without compensation, funds are required for meetings and for administrative facilities to effect the objectives of the board.

Several board committees in the field of animal science have sponsored the publication of useful reports, and committees dealing with the plant sciences have recently become affiliated with the board. One, the Committee on Preservation of Indigenous Strains of Maize in the Americas, is collaborating with the Technical Cooperation Administration and the Rockefeller Foundation. Another, the Committee on Plant and Crop Ecology, has subcommittees on aerobiology, agroclimatology, conservation, crop geography and vegetation analysis, plant crop yields, and plant diseases and pests.

The Agricultural Board, if properly implemented, can (1) mobilize the scientific talent of government, industry, and universities into committees competent to comprehend the broad problems of agriculture and the order in which they should be attacked; (2) collect facts and evaluate existing knowledge in relation to predictable results of present policies or practices in agriculture; (3) determine trends in current research and select neglected areas most likely to yield profitable long-range results; (4) disseminate knowledge and expedite the transition of research discoveries to applications in technological practice, governmental policies, or socioeconomic affairs.

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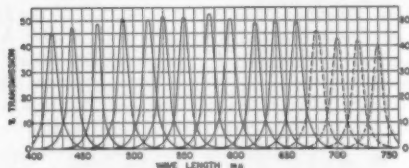
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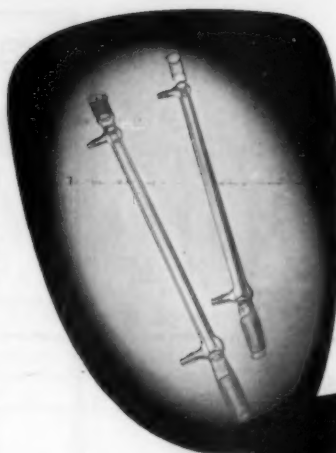
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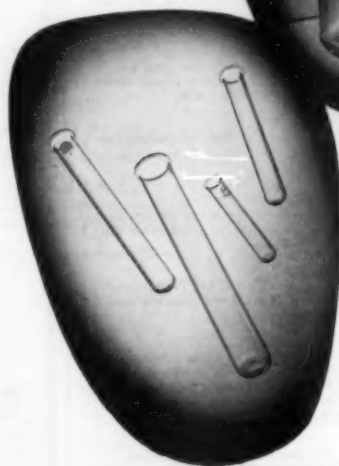
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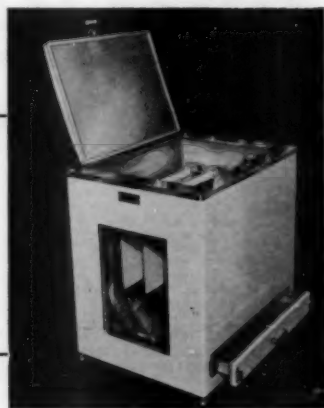
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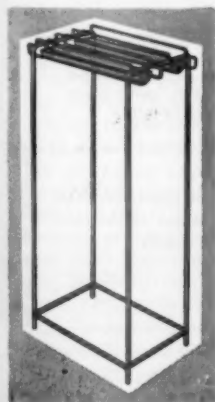
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# Microbial Selection

Vernon Bryson and Wacław Szybalski

*The Biological Laboratory, Cold Spring Harbor, New York*

ANY CONSIDERATION OF THE PROBLEM of microbial selection is inevitably linked with both the heterogeneity of microbial populations and the nature of resistance. Selection presupposes differences between cells, arising adaptively or by mutation. Appropriate use of the selective agent will change the average composition of a population, resulting in the establishment of new types, even to the complete exclusion of parent-type cells. Many experiments show that a so-called pure culture descended from a single cell eventually comes to consist of several different kinds of individuals unlike the remainder of the population. If the number of properties studied is large, each cell may be unique. Quantitative studies on variability are greatly simplified if the differences observed are discontinuous and have a genetic origin.

The extraordinary ecological flexibility of microorganisms enables certain of them to survive in the most unfavorable of habitats. Bacteria have been found growing at a pH of less than 1, and at temperatures exceeding 70° C. The list of chemical compounds utilized as sources of energy for biosynthesis continues to surprise the biochemist. Great variability, rapid reproduction, small size, and ease of environmental manipulation combine to make the controlled analysis of populations exceeding  $10^{10}$  individuals a feasible laboratory procedure. Yet obviously we cannot examine  $10^{10}$  cells one by one. It is here that selection enters, based on differences in the level of resistance of individual cells to the selective agent, and allowing in favorable instances the elimination of all but a small fraction of the population. For example, in the presence of certain bacteriophages or antibiotics, only one mutant bacterial cell in a sensitive population of approximately one billion may be able to survive and form a clone.

Sensitivity to toxic agents is one of the properties showing considerable variation within a group of microorganisms related by descent. Most often the different grades of resistance in natural populations are distributed in small steps over a limited concentration range of the agent. By continued selection, however, resistance may be shifted either upward or downward. Experimental methods devised to accomplish microbial selection must be fitted to the nature of the selecting agent. The choice of selective environments is almost limitless. Without detailed reference to a vast literature, attention is directed to such physical agents as radiation, temperature, desiccation, pressure, surface tension, and mechanical agitation.

The category of chemical materials available to establish selective pressures includes metallic ions, halogens, acids, alkalis, oxidizing and reducing agents, alcohols, phenols, dyes, and others too numerous to mention. Any chemical substance may belong to more than one group, and the distinction between physical and chemical agents is often arbitrary, with the possibility that common effects may be produced. Selection of x-ray- or ultraviolet-resistant *Escherichia coli* strains results in simultaneous resistance against many chemical agents affecting redox potential, and vice versa (1). The concept that related modes of action of toxic agents may be revealed through patterns of cross-resistance has many interesting implications (2).

Selective agents may in themselves be entirely or predominantly of biological origin, as exemplified by antibodies, bacteriophages, antibiotics, lysozyme, and the kappa substance in protozoa. Depending on the nature of the selective substance, we may recognize cellular fluctuations in resistance level contingent upon enzymatic differences, modifications in the composition of polysaccharide or other capsular investment layers, alterations in permeability, variations (hypothetical) in the configuration or distribution of virus and antibody receptor sites, and changes in electric charge—to list only a few. The ways in which biological variability may lead to opportunities for microbial selection are evidently vast.

Controversy still exists concerning the mode of origin of microbial resistance, a subject beyond the scope of these introductory comments on microbial selection and often dependent on the particular biological system being studied. A minority of investigators would attribute the increased concentration of drugs required for inhibition of consecutively treated cells to contact-induced resistance, rather than to selection. Obviously, adaptation and selection are not necessarily exclusive. Varied opinions still exist after investigators have attempted to amalgamate their own theories with nuggets of wisdom mined from the writings of Luria and Delbrück (3), Demerec (4), Hinshelwood (5), Sevag and Rosanoff (6), and Eagle *et al.* (7).

In common with investigations in microbial genetics elsewhere, research in our laboratory has been directed whenever possible toward the use of selective systems of the streptomycin type (4), wherein a relatively constant number of highly resistant cells may be isolated in a single experiment over a wide range in concentration of the drug. Here mutation rates are determined easily and quantitatively, even though the data

may represent a collective estimate of several genetic changes (8), particularly at intermediate drug levels. Sensitive cells in the population are simply eliminated. Described as facultative multiple-step resistance, as opposed to obligatory multiple-step resistance (8), the streptomycin pattern, to our knowledge, has been observed only in mycobacteria exposed to isoniazid by Szybalski and Bryson (9) and in staphylococci treated with micrococin by Markham *et al.* (10). Resistance of the streptomycin pattern is dependent on mutation, and permits selective isolation in the case of isoniazid of fully resistant strains in the complete absence of the drug (11) when the replica-plate method of Lederberg and Lederberg (12) is used.

Unfortunately for geneticists, but happily for physicians, the facultative multiple-step pattern and the one-step pattern of bacterial resistance are rare. Resistance to most agents, including those used in chemotherapy, follows the obligatory multiple-step pattern, as noted in the isolation of penicillin-resistant strains (13). This means that most antibiotics will eliminate all the members of a bacterial population if used initially in high concentration. It also means that special methods for the selection of such resistant strains may be necessary, permitting drug concentrations inhibitory to the general population but allowing multiplication of mutants with small factors of resistance.

Table 1 represents a survey of the principal methods generally applicable for isolating resistant microorganisms, including use of the turbidostatic selector and the gradient plate to be described later.

Only the direct methods are practical for the derivation of resistant strains. Indirect methods have been intended to demonstrate the spontaneous origin of resistant mutants (replica-plate) or have emerged incidentally in studies of the nature of variations in

sensitivity. Specialists concerned directly with problems of microbial selection and resistance will be interested in the observation that with more than 50 antibiotics studied in this laboratory it has always been possible to isolate bacterial strains either more sensitive or more resistant than the parent culture. Any strain may have different levels of resistance, depending on the species or variety of organisms. One may, however, anticipate the existence of certain naturally occurring strains that are so close to the potential upper or lower level of resistance that modifications through artificial selection may be made at first in one direction only.

## Part I: Gradient Plate Technique for Study of Bacterial Resistance<sup>1</sup>

Waclaw Szybalski

FOR extensive studies of patterns of bacterial cross-resistance (2) it has been necessary to devise a simpler and more efficient method of isolating strains resistant to a large variety of antibiotics. Previous methods, based either on serial dilution or on the use of an agar plate in contact with a reservoir of antibiotic, present certain disadvantages.

In serial dilution methods concentration of the chemical agents increases stepwise; and if the concentration steps are not kept close together it is easy to miss the proper dilution range, which is often very narrow. When a scarce antibiotic is used, it is possible only within relatively narrow limits to decrease the volume of nutrient and thus conserve the chemical. In doing so, one also decreases the size of the bacterial population and reduces the chance of isolating resistant mutants. Another shortcoming of these methods is their waste of labor and materials; generally, only one plate or tube of the series is useful, and the rest are discarded.

Continuous increase of the antibiotic concentration is the advantage of methods based on the use of an agar plate in contact with a reservoir of antibiotic solution, such as an assay cylinder, paper disk, or "gutter plate" (14). In this case, however, the concentration gradient represents a steep logarithmic function. The areas of appropriate concentration are usually very narrow and may move rather rapidly during the experiment, owing to diffusion.

For these reasons we have tried to develop a method (15) that will allow the preparation of an agar plate with a very gradual proportional increase of the antibiotic concentration along one horizontal axis—the gradient axis. Plates are poured with two layers of agar (Fig. 1). The bottom layer consists of 20 ml plain nutrient agar, allowed to harden with the plate slanted sufficiently so that the entire bottom is just covered. With the dish in the normal horizontal position, another 20 ml of agar is added, containing the

<sup>1</sup> Aided by a research grant from the National Tuberculosis Association.

TABLE 1

### METHODS OF ISOLATING RESISTANT STRAINS

| I. Direct methods (in the presence of the toxic drug)   |                               |                                |
|---|-------------------------------|--------------------------------|
| Increase of drug concentration  | Medium                        |                                |
|   | Liquid                        | Solid                          |
| Stepwise  | Serial dilutions (test tubes) | Serial dilutions (agar plates) |
| Continuous  | Turbidostatic selector        |                                |
| Nonproportional   | + direct feeding system       | Reservoir agar-plate           |
| Proportional  | + proportional feeding system | Gradient agar-plate            |
| II. Indirect methods (in the absence of the toxic drug)   |                               |                                |
| Examples  |                               |                                |
| Replica-plate method (12)   |                               |                                |
| Selection by associated characters (e.g., rate of growth, resistance to other agents related by cross-resistance) |                               |                                |
| Selection at random   |                               |                                |

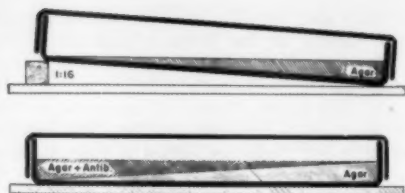


FIG. 1. Method of preparing a gradient plate.

appropriate concentration of toxic agent. Downward diffusion of the drug, which in this way becomes diluted in proportion to the ratio of the thicknesses of the agar layers, establishes a uniform, linear concentration gradient during subsequent incubation. The drug may also be incorporated in the bottom layer, and by changing the ratio of its concentrations in both layers it is possible to adjust the range and the slope of the gradient, which remains surprisingly stable for several days after the preparation of the plate. When heavy bacterial suspensions are incorporated in the top layer, or else streaked or spread over the agar surface, only the resistant cells are able to form colonies beyond the boundary of confluent growth; and if the resistant colonies are streaked out on the same plate, the resistance may be verified and further increased (Fig. 2). In this way one plate may be sub-

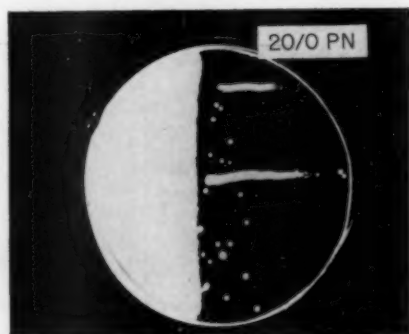


FIG. 2. Gradient plate. Bottom layer—nutrient agar; top layer—nutrient agar + penicillin (20  $\mu$ g/ml). Surface seeded with a suspension of *E. coli*, strain B/r. Only resistant cells develop colonies beyond the boundary of confluent growth. Two of these resistant colonies are streaked out. Note the formation of second-step resistant colonies at the end of the streaks.

stituted for several series of dilutions, increasing resistance over more than one step. Resuspension of the resistant colonies in broth, with or without subsequent incubation, and further plating on gradient plates with a higher concentration of the toxic agent, have been used to develop strains of *E. coli*, *M. pyogenes* var. *aureus*, and *Mycobacterium ranae* that are resistant to over fifty chemotherapeutic agents.

With the use of small, autoclaved artist's brushes or glass capillaries, as many as ten streaks of the standardized bacterial suspensions can be placed

parallel to the concentration-gradient axis on one gradient plate. The same method allows easy comparison of the sensitivities of various strains to a given drug, since the length of the growing streaks is a direct measure of the inhibitory concentration of the drug (2) (Fig. 3). The shape of the streaks per-

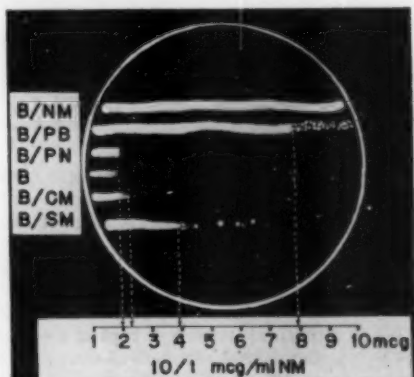


FIG. 3. Measurement of bacterial sensitivity. Neomycin is incorporated in both agar layers—10  $\mu$ g/ml in the top, and 1  $\mu$ g/ml in the bottom layer. Suspensions of *E. coli* consisting of the parent strain B and strains resistant to neomycin B/NM, polymyxin B B/PB, penicillin B/PN, chloramphenicol B/CM, and streptomycin B/SM are streaked over the surface of the gradient plate. In the example the approximate inhibitory concentrations in  $\mu$ g/ml are: 2 (B and B/PN); 2.3 (B/CM); 4 (B/SM); 8 (B/PB); 10 (B/NM).

mits visual distinction of different patterns of inhibition (Fig. 4). Gradual inhibition may indicate that the toxic agent interferes with a simple chemical reaction of a low kinetic order. Abrupt inhibition suggests interference with a mathematically high-order reaction, represented, for instance, by a chain of consecutive reactions. It seems to be important, in describing an antibacterial agent, to consider not only the inhibitory concentration, but also the pattern of inhibition.

Among the potential applications of the gradient-plate method we may mention the simple assay of antibacterial drugs and the study of microbial growth factors.



FIG. 4. Examples of inhibition patterns.

Another approach to the problem of providing a proportionately increasing concentration of toxic agent using liquid media has been made by Bryson in this laboratory by means of a mechanical device (the turbidostatic selector), to be described in Part II.

## Part II: The Turbidostatic Selector— A Device for Automatic Isolation of Bacterial Variants

Vernon Bryson

IN RECENT years several investigators have worked on the problem of continuous bacterial cultivation. Apparatus designed to keep bacteria growing for indefinite periods has been described by Sims and Jordon (16), Levin (17), Savage and Florey (18), Kautsky and Kautsky (19), Gerhardt (20), and others. In the device of Monod (21) and that of Novick and Szilard (22), the population of bacteria is kept at a constant density by limiting the concentration of some essential growth factor supplied continuously in small quantities to the culture. This results in the attainment of a dynamic steady state at less than the normal growth rate, with culture volume maintained by a self-leveling overflow. In most of the equipment designed up to the present time, including the chemostat of Novick and Szilard, emphasis has been directed to supporting the bacterial population by continuous addition of a chemical environment of constant composition.

For some time we have been interested in making an apparatus for the cultivation of bacteria in a continuously or intermittently changing environment (23). The device has been named the turbidostatic selector (Fig. 5). The two essential components are a simple electronic circuit controlling periodic addition of nutrient to microorganisms whenever the culture reaches a fixed turbidity; and a proportional-feed system for increasing the concentration of some toxic substance, at a geometric rate, in the nutrient delivered automatically to the growth tube in response to reproduction of the cells.

Bacteria in the growth tube are kept at constant temperature. Culture turbidity is continuously measured by a standard system of two photovoltaic cells, balanced against each other in a potentiometer circuit, as in a conventional colorimeter. Every time turbidity exceeds the preset value, the galvanometric relay system opens a solenoid-operated pinch clamp, and fresh nutrient is added to the culture, decreasing its turbidity until the circuit is again balanced. Culture volume is kept constant by a self-leveling overflow.

The operation of the electronic circuit is controlled by current from a light box supported above a magnetic stirrer by metal legs, and containing the growth tube (Fig. 5, B). A light beam, entering this box from the lamp (Fig. 5, A), is split with a mirror. One portion of the entering beam passes directly through the

growth tube and onto the variable output photocell. Another portion of the beam is deflected at right angles by a mirror and is directed to the constant-output photocell. As bacteria multiply in the growth tube, less light passes through to reach the variable-output photocell. Countercurrent from the constant-output photocell therefore causes a rise in current passing from the light box to the control box. The latter unit, not visible in Fig. 5, contains the transformers, relays, and galvanometer required to operate the pinch clamp solenoid and regulate the temperature of the culture. Construction details are cited elsewhere (24). Current entering the control box passes directly

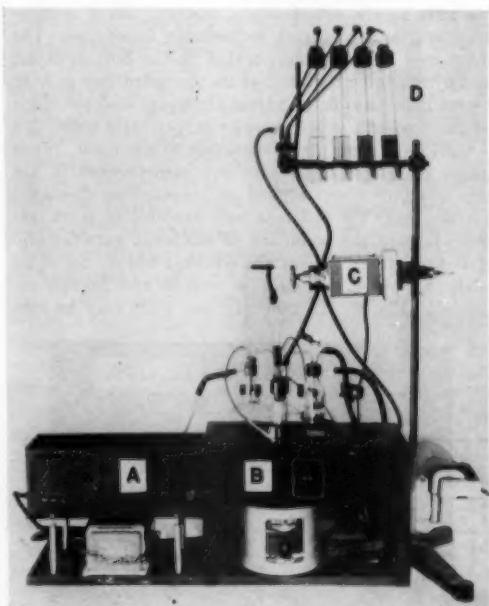


FIG. 5. The turbidostatic selector. (A) lamp; (B) light box containing growth tube and photovoltaic cells; (C) solenoid-operated hosecock; (D) proportional-feed system.

to an enclosed lamp-type galvanometer, shunted to give a sensitivity of about 20 mm/ $\mu$ a, and with the ground-glass scale removed. As bacteria grow in the light box, the rise in current reaching the galvanometer causes its beam to move horizontally and to leave the galvanometer through the aperture made by removing the ground-glass scale. At an optical density corresponding to an arbitrary cell titer, the galvanometer beam enters a photorelay.<sup>2</sup>

Closure of an a-c circuit by the photorelay activates a cumulative counter and the solenoid-operated hosecock (Fig. 5, C). Rubber tubes passing under the baseplate of the hosecock are thus opened, allowing sterile air to bubble into the proportional feed (Fig.

<sup>2</sup> Model 904185 BX, Photobell Co., New York City.

5, D), mixing the liquid and preventing entrance of contaminating microorganisms with the fall of fluid level. Nutrient siphons downward from the proportional feed into the growth tube, and excess culture passes through a constant-level siphon leading from the growth tube into a waste bottle. The resulting dilution of cells and decrease in optical density of about 2 per cent move the beam off the photorelay, and the cycle is repeated only if and when adapted or mutant elements of the population are able to grow within the increasingly rigorous selective environment. The upper limit of turbidity may be set with the potentiometer. Evolutionary change is automatically controlled by the increases in selective pressure, dependent on the genetic or adaptive potential of the microbial population, expressed as continued growth in the presence of a changing environment.

The proportional feed (Fig. 6) consists of four

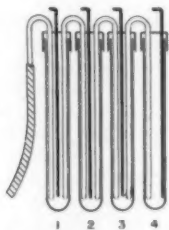


FIG. 6. Detail of proportional feed. Heavy lines represent stainless steel aeration tubes. Toxic agent and nutrient are withdrawn from rubber tubing connected to tube #1.

screw-cap test tubes connected by siphon bridges. Nutrient in each tube contains a dilution of toxic substance present in the tube to its right. The usual difference in concentration between adjacent tubes is tenfold, illustrated for graphic purposes by dye in Fig. 5. In actual use, the proportional-feed tubes must be optically identical and more translucent than the cell suspension in the growth tube.

The toxic agent and added nutrient are not titrated directly into the growth tube from a single vessel, because the concentration gradient available by titration results in an unduly steep rise of selective pressure in the growth tube. As a comparative example of concentration gradients obtainable by different methods, we may first consider the result of titration or direct-feed (Fig. 7). The data represent dye samples taken from a receiving vessel acting as the growth tube and containing 30 ml of phosphate buffer at pH 6.7. A solution of buffer containing neutral red reading 55.1 in the Fisher colorimeter (525 filter) was added to the receiving vessel in 20-ml quantities. After each addition, the contents of the receiving vessel were again reduced to 30 ml, and the withdrawn 20-ml sample was measured colorimetrically. Nine consecutive samples gave the titration curve shown in Fig. 7. As more samples were taken, the final concentration approached a value of 55.1. In the chemostat of Novick and Szilard, a chemically constant concentra-

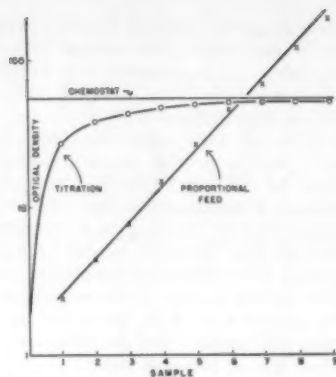


FIG. 7. Density measurements of dye samples, indicating concentration gradients obtainable by methods described in the text.

tion of limiting nutrilit is added to the growth tube. For purposes of comparison, the chemostat curve is represented in Fig. 7 as equivalent to the original concentration of dye added in the titration experiment. With continued sampling, the chemostat and titration curves should become experimentally indistinguishable.

In modifying the bacterial environment by increasing the concentration of a toxic substance, the titration curve is not as useful as a geometric increase of the type  $y = a \cdot b^x$ . The geometric increase observed in Fig. 7 may be considered as an approximate calibration of the proportional-feed system. In obtaining the data, a 0.5 per cent tincture of neutral red in 50 per cent alcohol was distributed in the four proportional-feed tubes as follows: The tube farthest from the siphon outlet (Fig. 6, #4) received 0.7 ml of dye solution, and each adjacent tube received one tenth the concentration of the tube distal to it with respect to tube #1. Each tube contained approximately 50 ml of buffer (pH 6.7), with 30 ml in the growth tube. Consecutive 20-ml samples were drawn from the terminal proportional-feed tube into the growth tube, again withdrawn after mixing, and then measured with a green filter in the colorimeter. In other experiments it is seen that, if the factor increase between proportional-feed tubes is decreased to 5 or less, the curve tends to become sigmoid.

A single vessel may be substituted for the proportional feed when a decreasing concentration gradient is required—for example, in the isolation of prototrophs by diluting out the required nutrilit supporting growth of an auxotroph. In such an experiment complete medium in the growth tube would be periodically diluted by direct feed of minimal media. The selector may also be operated as a chemostat without the restriction of a limiting growth factor.

As auxiliary equipment, the selector is provided with a rescue system that will deliver pure nutrient to the culture at timed intervals, independent of the rate of growth. Nutrient from the rescue system is



not sufficient to provide entirely for growth at a rate exceeding 20 per cent of the normal growth rate. Therefore, unless the reproducing cell population is very small or is growing very slowly, it will continue to activate the proportional feed. The rescue system serves to dilute out toxic agent introduced from the proportional feed to provide repeated opportunities for selection. Its use may be required when the toxic agent produces a bacteriostasis that effectively prevents selective growth, resulting in a complete cessation of activity. The culture is aerated by humidified air blown over the surface and maintained at 37° C by a heating element inserted in the centrifuge carrier holding the growth tube. Cells are mixed by a magnetic stirrer, and samples may be withdrawn at will by aspiration into an attached vial.<sup>3</sup>

To understand the process of automatic evolution it is necessary to recall that many toxic agents are not equally harmful to all the individuals of a bacterial population. As more toxic chemical is added in nutrient from the proportional feed, bacterial growth is reduced and a process of artificial selection is begun. A point is reached when the general level of population can no longer increase. If resistant mutants or variants are present in the general population, and can grow, they alone will contribute to added population density and an increasingly rigorous environment will result. The exponential nature of the concentration gradient results in a continued selective process, with the increase of selection pressure always proportional to the concentration of toxic agent already attained. A gradual increase in the toxicity of the environment is of relatively great significance in attainment of the penicillin pattern, as opposed to the streptomycin pattern of resistance (25).

Several types of experiments may be performed by the selector without more than occasional attention from the operator. The present design does not permit the use of toxic agents that reduce light transmission; and the rate of flow from both proportional-feed and rescue systems tends to diminish if unadjusted during the progress of an experiment. Some of these difficulties can be overcome by modified design. To facilitate the derivation of quantitative information from the instrument, it is being equipped with a recording time stamp in place of the cumulative counter, to indicate the exact moments of operation of the hose-cock. Another timer will hold the hose-cock open for one minute at each operation.

Our present efforts are directed toward the isolation of bacteria resistant to antibiotics and germicidal agents. It is at once seen that some agents are more suitable for use in the selector than others. With *E. coli* (strain B), penicillin resistance has been increased two- to fourfold, whereas over a seventyfold increase is possible. Increased resistance by a factor of 16 was obtained by employing neomycin in one ten-day run of the instrument. Without use of the rescue system, a zephiran-resistant strain of *E. coli* (B/ZS) was iso-

<sup>3</sup> Acknowledgment is due to Wacław Szybalski for several useful suggestions.

lated by the selector in three days. It proved to be no more sensitive to this quaternary ammonium compound than the stock laboratory strain (B/Z #10) obtained by ten consecutive isolations from broth containing the highest tolerable concentration of drug (Table 2). Cells were grown for 48 hours at 37° C.

TABLE 2  
PERCENTAGE OF VIABLE *E. coli* AFTER GROWTH IN  
NUTRIENT BROTH CONTAINING ZEPHIRAN,  
AS COMPARED WITH CONTROL

|                | Zephiran concentration |               |               |               |              |
|----------------|------------------------|---------------|---------------|---------------|--------------|
|                | 1/<br>64,000           | 1/<br>128,000 | 1/<br>256,000 | 1/<br>512,000 | Con-<br>trol |
| Strain B       | 0                      | 0.00006       | 14            | 103           | 100          |
| Strain B/ZS    | 0                      | 1.4           | 51            | 67            | 100          |
| Strain B/Z #10 | 0                      | 0.01          | 25            | 33            | 100          |

Certain toxic substances may prove to be unsuited for use in the selector because, at the exact level of bacteriostasis, the metabolic activity of the majority of cells is able to exhaust essential substrate materials and effectively suppress the emergence of clonal mutants or adapted populations better fitted for survival. Obviously, where growth depends on the presence of bacterial mutants, the population size should exceed the reciprocal of the mutation rate. Since the number of cell divisions per unit increase in toxic concentration may affect the pressure of selection, experiments are now being initiated in which an aspirator bottle containing 3 liters of nutrient is placed between the proportional feed and the culture. The aspirator bottle and proportional feed are placed at the same height, and connected by siphons so that their fluid levels drop simultaneously. A more gradual increase of toxic agent is thus attainable. Present experience indicates that for the empirical isolation of antibiotic-resistant mutants, the instrument is not as effective as the gradient plate method (2, 26).

Some potential applications of the turbidostatic selector involve the graphing of cyclical activity of the proportional feed to aid in distinguishing the relative importance of adaptation and mutation-selection as factors in adjustment to a toxic environment. Other possibilities include basic studies of mutation rate; the determination of modified resistance in bacterial populations undergoing little or no multiplication; the analysis of cell physiology at the exact level of bacteriostasis; studies of the comparative resistance of mixed bacterial populations to inhibitory or stimulating chemicals and metabolites; isolation of strains metabolizing foreign substrates by gradual substitution of materials in the proportional feed; and the derivation of partial or multiple-step reverse mutants.

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## News and Notes

### American Documentation Institute

THE American Documentation Institute (of which the AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE is a nominating agency) held a two-day annual meeting in the Coolidge Auditorium of the Library of Congress Feb. 26-27. The principal elements of the program were symposia on microfacsimile reproduction and on the rationalization of subject controls, and a discussion of current issues in documentation. There was also a comprehensive exhibit of apparatus applicable to documentary reproduction, projection, transmission, and other techniques of documentation.

The live issue before the meeting was whether the institute, the membership of which had up to then been composed exclusively of delegates nominated by 69 institutions and professional societies, should throw its rolls open to personal and other institutional memberships, and whether it should at the same time become a dues-paying organization.

For some time there has been growing evidence of the need for an organization in which members of different professions who are engaged in documentation, including information officers for scientific and technical organizations, archivists, and librarians, can find a common meeting place for discussion and collaboration. The need is evident in recent communications to this journal by William F. Hewitt, Jr., and Samuel A. Miles (*SCIENCE*, **114**, 134, 554 [1951]), as well as in the program at the Philadelphia meeting of the AAAS, sponsored by several of its sections under the title "Operation Knowledge" (*ibid.*, **115**, 178 [1952]).

On all points the issue was resolved in favor of liberalizing the membership requirements for ADI. Personal and institutional members will be admitted on equal terms with present and future organizational delegates. As soon as 100 persons and institutions have signified their intention of seeking membership on the new terms, a meeting will be called to consider constitutional changes.

The new officers elected include Luther H. Evans (Librarian of Congress), president; Milton O. Lee (Federation of American Societies for Experimental Biology), vice president; Watson Davis (Science Service), treasurer; and G. Miles Conrad (Library of Congress), secretary.

VERNER W. CLAPP

*Library of Congress  
Washington, D. C.*

### Scientists in the News

Frank W. Abrams, chairman of the board of the Standard Oil Company (New Jersey), has been elected to the Ford Foundation's Board of Trustees. Mr. Abrams will continue to serve as chairman of the Fund for the Advancement of Education for the next six to eight months. Henry Ford II is serving as acting president of the Foundation while Paul G. Hoffman, president, is on temporary leave of absence.

Andrew W. Anderson, chief of the Fish and Wildlife Service's Branch of Commercial Fisheries, has been designated deputy administrator of the Defense Fisheries Administration. Mr. Anderson will assume his new duties in addition to his present assignment for the duration of the DFA program. Milton C. James, who retired as assistant director of the service on Mar. 31, served as DFA deputy administrator from its formation until his retirement. Under a reorganization of DFA effected in December 1951, Mr. Anderson took on additional duties as chief of the Office of Operations.

Eugene C. Bovee has been appointed associate professor and acting head of the Department of Zoology and Physiology at North Dakota Agricultural College. Dr. Bovee has been on the staff of the California State Polytechnic College of San Luis Obispo.

Ralph C. Bryant, of Fort Collins, Colo., has been appointed professor of forest economics in the North

Carolina State College School of Forestry. Dr. Bryant has been head of the Department of Forest Management at Colorado A & M College.

**C. J. B. Clews**, principal scientific officer at Great Britain's National Physical Laboratory since 1948, has accepted appointment to the chair of physics in the University of Western Australia. He succeeds **A. D. Ross**, who joined the university faculty immediately after it was founded in 1912, and who is retiring after 40 years of continuous service as teacher, investigator, and administrator.

The American Diabetes Association was represented by **J. Richard Connelly**, its executive director, at the first international congress of the International Diabetes Federation, which met in Leiden July 7-12. Among the American authorities attending the congress were **Frank N. Allan**, president of the association; **Charles H. Best**, of Toronto; **Elliott Joslin**, honorary president of the association, and **Hugh L. Wilkerson**, chief, Diabetes Section, USPHS.

**Dorothy Day**, recently of the Biology Department of MacMurray College, has joined the staff of Alaka Research Laboratories Division of Laequer and Chemical Corporation, Brooklyn. She will serve as microbiological consultant in the moisture- and fungus-proofing program carried on for the Bureau of Ordnance, Department of the Navy.

The following appointments have been made in the University of London: **W. R. Dean**, lecturer in mathematics in the University of Cambridge, to the Goldsmid chair of mathematics tenable at University College; **H. C. Longuet-Higgins**, reader in theoretical chemistry in the University of Manchester, to the University chair of theoretical physics tenable at King's College. The title of reader has been conferred on **H. R. Allen** and **J. W. H. Holmes** (veterinary medicine), **G. H. Arthur** and **G. C. Knight** (veterinary surgery), in the Royal Veterinary College.

At the invitation of the Japanese government, the Fish and Wildlife Service has despatched **Francis M. Fukuhara** to accompany a Japanese salmon fishing expedition operating in the Bering Sea. Mr. Fukuhara, a native of Seattle, Wash., and a student at the Fisheries School of the University of Washington, joined the *Tenyo Maru* No. 3, and will work with the Japanese fleet in the collection of scientific data on the composition and distribution of the salmon populations of the north Pacific Ocean.

**George Glockler**, of Iowa City, has joined the staff of the Office of Ordnance Research as director of the Division of Chemical Sciences. Dr. Glockler is on leave of absence from the University of Iowa, where he has been head of the Department of Chemistry and Chemical Engineering since 1940. A specialist in the field of electrochemistry, Dr. Glockler is a member of the NRC Subcommittee on Insulation.

**William Hume II**, until recently assistant director

and physicist with the Research and Development Division of New Mexico Institute of Mining and Technology, has been made director of the College Division of the institute. **John Harty**, formerly head of the Department of Physics and Geophysics, has been appointed principal physicist of Research and Development Division. Replacing him as head of the Department of Physics and Geophysics is **Marvin H. Wilkening**, associate professor of physics.

**Kalevi A. Kirvenniemi**, General Survey Office, Finland, and **Per L. Sondena** and **Anders Grydeland**, of Widerøes Flyveselskap and Polarfly A/S, Oslo, were recent visitors at the Atlantic Regional Headquarters of the U. S. Geological Survey.

The American Physical Therapy Association has elected **Harriet S. Lee** as its president. Colonel Lee, chief of the physical therapy section of the Army's Office of the Surgeon General, will hold office for two years.

**Albert L. Lehninger**, associate professor of biochemistry and associate professor at the Ben May Laboratory for Cancer Research at the University of Chicago, has been appointed DeLamar professor of physiological chemistry at The Johns Hopkins University School of Medicine. He succeeds **William Mansfield Clark**, who retired at the end of this academic year from the endowed chair he has held since 1927. Dr. Clark has accepted a new appointment as research professor in chemistry at the Homewood campus of Johns Hopkins. Dr. Lehninger is in Europe completing a year's study under a Guggenheim traveling fellowship.

**Katharine E. McBride**, president of Bryn Mawr College, has been elected chairman of the board of trustees of the Educational Testing Service. She has been a trustee of the service since it was formed in 1948 in the merger of the testing activities of the American Council on Education, the College Entrance Examination Board, and the Graduate Record Examinations of the Carnegie Foundation. Dr. McBride succeeds **Henry H. Hill**, president of the George Peabody College for Teachers, as board chairman. New trustees are **Frank H. Bowles**, **Lewis W. Jones**, and **George D. Stoddard**.

**H. R. Murdock** has joined the Johnson & Johnson Research Foundation. During the past year Dr. Murdock worked under a postdoctorate fellowship at the University of Buffalo, from which he received his Ph.D. in physiology and pharmacology in 1951.

**Russell A. Nelson** has been named director of the Johns Hopkins Hospital and will assume his new position on Sept. 1. He will succeed **Edwin L. Crosby**, director of the hospital since 1946, who has resigned to become executive head of the newly created Joint Commission for the Accreditation of Hospitals. Dr. Nelson, at present assistant to **Lowell J. Reed**, vice president of the Hopkins University and Hospital, has been associated with the medical institutions since his

graduation from the Hopkins School of Medicine in 1937.

After a half-century of teaching, **William L. Prager**, professor of chemistry at New York City College, has retired, having reached the mandatory retirement age of 70 years.

**Herbert F. Roemmele** has been installed as president of the New York Chapter of the New York State Society of Professional Engineers. For the past 25 years Professor Roemmele has served on the faculty of Cooper Union's School of Engineering, where he is professor of mechanical engineering and dean of students. Since 1948, he has also served as director of industrial relations at the Cooper Union.

**Robert P. Sharp**, professor of geomorphology, has been appointed chairman of the Division of Geological Sciences at California Institute of Technology. He succeeds the late **Chester Stock**, who died in 1950.

**Denzel D. Smith** has been appointed head of the Personnel and Training Branch of the Psychological Sciences Division, ONR. Prior to his appointment to the Office of Naval Research he was professor of psychology at the University of Maryland and director of the university's Counseling Center. **Marguerite Young**, formerly acting head of the Personnel and Training Branch, has accepted a position in the Biological Sciences Division, National Science Foundation.

**Marian W. Smith** has resigned as secretary of the AAAS Section on Anthropology (H) and her position with the Department of State to take up residence in England as Mrs. H. F. Akehurst. She will retain her membership in the Association and plans to further anthropological research on both sides of the Atlantic. Currently she is editing the papers presented in the Section H symposium at Philadelphia, on Prehistoric and Historic Asia: Trans-Pacific Contacts with the New World, to be published as a memoir of the Society for American Archaeology, with support from the Wenner-Gren Foundation for Anthropological Research (SCIENCE, 115, 670 [1952]). **Gabriel Lasker**, of Wayne University College of Medicine in Detroit, has been appointed by the AAAS Executive Committee to complete Dr. Smith's unexpired term as secretary of Section H.

**Thomas P. Thayer**, of the U. S. Geological Survey, in recognition of his work on the geology of the Bomi Hills iron deposits, Liberia, has been made a Commander of the Star of Africa. The order was conferred by President Tubman in Monrovia. Dr. Thayer returned to the U. S. in mid-June. **W. D. Johnston, Jr.**, chief of the Foreign Geology Branch, has been made an officer in the Order of the Southern Cross (Cruzeiro do Sul), in recognition of his geological work in Brazil.

**Frans Verdoorn**, editor of *Chronica Botanica* and chairman of the International Phytiohistorical Commission, Waltham, Mass., has been elected a Cor-

responding Member of the Royal Netherlands Academy of Sciences, Amsterdam.

**Karl Wilbur**, professor of zoology at Duke University, has been given a leave of absence to serve as physiologist with the Biology Branch, Division of Biology and Medicine, U. S. Atomic Energy Commission.

**Richard J. Winzler**, professor of biochemistry and nutrition at the University of Southern California School of Medicine, has been appointed professor and head of the Department of Biological Chemistry at the University of Illinois College of Medicine.

## Education

California Institute of Technology has promoted the following staff members to full professorships: **Pol E. Duwez** (mechanical engineering), **Robert B. King** (physics), **Paco Lagerstrom** (aeronautics), and **Charles F. Rieghter** (seismology). New associate professors are **Norman Davidson** (chemistry), **Renato Dulbecco** (biology), **Peter Kyropoulos** (mechanical engineering), and **Charles H. Wilts** (electrical engineering). **Matthew Sands** and **Ward Whaling** (physics) were named assistant professors.

Fourteen fourth-year **Duke University** medical students have left for three months' work in English hospitals. Most of them will work in three London hospitals: **St. Mary's**, **Guy's**, and **St. Bartholomew's**. The others will do work in pediatrics under **James Spence** in New Castle.

India's **Five Year Development Plan** has among its objectives the rebirth and further development of Indian culture. Emphasis will be laid on imparting necessary skills to large numbers of people and on promoting higher standards of efficiency in order that each individual may contribute effectively to the productivity and economic well-being of the nation. Most important item is considered to be the provision of free universal compulsory education for all children between the ages of 6 and 14. Adult education will receive its share of attention through the Social Education Program and the Education Caravan. When the caravan visits a village, it sets up its mobile stage, motion-picture theatre, and two exhibition halls and produces plays, gives concerts, shows educational and cultural films, and in general seeks to motivate the villagers toward gaining at least rudimentary education. The Education Ministry is organizing audio-visual units to take films and film strips all over India, and the production of educational films is being subsidized. To cope with the great demand for scientists and technicians, existing institutes are being enlarged, and four large new ones are being built. Two of these, the Institute of Technology at **Karagpur**, and the Eastern Higher Institute at **Hijli**, are already in operation.

**Hahnemann Medical College** dedicated a new virus laboratory in May in honor of **Joseph A. Langbord**,

medical director of the Sidney Hillman Medical Center of Philadelphia. The Goldman Isotope Laboratory was officially dedicated last month at a banquet at which Ralph T. Overman, of Oak Ridge Institute of Nuclear Studies, was the principal speaker.

At **Illinois Institute of Technology**, Van V. Alderman and Arthur G. Keenan have been appointed assistant professors of chemistry, and Frank L. Holloway, of the University of Illinois, has been appointed an organic research chemist of Armour Research Foundation. Lester R. Ford, chairman of the Mathematics Department, past president of the Mathematical Association of America, and a former editor of the *American Mathematical Monthly*, has retired after 15 years at Illinois Tech. As a lecturer at the University of Edinburgh in 1914 and 1915, he was the first American to hold a teaching position in a Scottish university.

Five professors at **Northwestern University** will retire Sept. 1. They include: Kenneth W. Colegrove (political science); Elton J. Moulton (mathematics); Karl A. Meyer (surgery—and medical superintendent of Cook County Hospital); Arthur Metz (surgery—and chief surgeon for the Chicago, Milwaukee, St. Paul & Pacific Railroad); Frederick W. Merrifield (oral surgery).

**Ohio State University** has appointed Arthur W. Foshay, of Teachers College, to the directorship of its Bureau of Educational Research, succeeding T. C. Holy, who has retired. Hamilton B. G. Robinson, of OSU's College of Dentistry, and president of the City Board of Health, has been appointed associate dean of the college. Leontine R. Young, of the New York School of Social Work, has been appointed a professor in Ohio State's School of Social Administration.

## Grants and Fellowships

**Vanderbilt University School of Medicine** has appointed the following new staff members: Robert I. Carlson and John William Hillman (surgery); Elliot Voss Newman (experimental medicine); and Charles Rawlinson Park (physiology). Paul D. Lamson, professor of pharmacology and head of the department, and Charles S. Robinson, professor of biochemistry, have reached emeritus status.

The **Oliver E. Buckley Solid State Physics Prize**, consisting of an annual prize of \$1000, has been established by Bell Telephone Laboratories and will be awarded by the American Physical Society to the person adjudged to have made a most important contribution to the advancement of knowledge in solid state physics within the five years immediately preceding the award. Named in honor of the laboratories' former president, now board chairman, who is to retire Sept. 1 after 38 years of active service, the prize is endowed by a trust fund of \$50,000. In 1978 the remaining funds are to be turned over to the American Physical Society for its own use. The first

winner will be selected by a committee consisting of Harvey Brooks, J. B. Fisk, J. C. Slater, Cyril S. Smith, and J. H. Van Vleck.

The **Jane Coffin Childs Memorial Fund for Medical Research** has appropriated \$264,080 for support of cancer research projects and fellowships beginning in 1952 and extending, in some cases, to 1956. Largest grant (\$123,500) went to the Ben May Laboratory for Cancer Research, of the University of Chicago Medical School, for a five-year investigation of the hormonal control of human cancer under the direction of Charles B. Huggins. Helen W. Toolan, Sloan-Kettering Institute, received \$15,000 for further experiments on the growth of human tumors in animals. The following fellows will receive one year's support: Melvin Fried, Cambridge University; Frederic L. Hoch, Massachusetts General Hospital; Martin Lubin, MIT; and Barbara E. Wright, Carlsberg Laboratory.

The **Endocrine Society** has announced the following awards: Squibb Award for meritorious contributions to endocrinology to James H. Means, of Harvard; the Ciba Award to Seymour Lieberman, of Columbia; the Schering Fellowship for 1951 to Claiborne L. Courtright, of Oklahoma Medical Research Institute (because of the original recipient's being called to military service); and the Ayerst, McKenna and Harrison Fellowship for 1952 (\$5000) to John C. Laidlaw, of Peter Bent Brigham Hospital, Boston.

Cornell University's Social Science Research Center has established a series of graduate fellowships in the behavioral sciences with a \$50,000 fund drawn from a grant made to the university by the **Ford Foundation**. About 20 fellowships will be awarded over a four-year period beginning next fall, and the stipends will range from \$1600 to \$2400, with up to \$700 additional for tuition, fees, or travel. Inquiries should be addressed to the Fellowship Committee, 206 Morrill Hall, Cornell.

The **Guggenheim Foundation** has appointed 15 new Daniel and Florence Guggenheim Jet Propulsion Fellows at Princeton and Caltech to carry on basic research in the development of commercial and scientific applications of jet and rocket propulsion.

The **National Society for Crippled Children and Adults** and **Alpha Gamma Delta**, international women's fraternity, are sponsoring a four-week training course at the Institute of Physical Medicine and Rehabilitation of the New York University-Bellevue Medical Center, July 7-Aug. 1. Eighteen graduate fellowships for this special training have been awarded to persons in the U. S., Canada, and Switzerland.

The **New York Foundation** has made a grant of \$28,000 to Sea View Hospital, on Staten Island, for research studies of the new antituberculosis drugs. Tests of the drugs were begun there last September, and the grant is specifically to fill the hospital's needs for additional personnel to conduct more extensive



laboratory tests. The research program at Sea View is under the direction of George G. Ornstein, Edward H. Robitzek, and Irving J. Selikoff.

**Research Corporation** has allocated \$170,000 for research during the past quarter. Of this amount, \$72,000 was in the form of General Grants, supporting research primarily in the physical sciences. The remainder was distributed under the Cottrell Grants program.

**Sharp & Dohme** has made a grant in support of the work of Maurice S. Segal, Tufts College Medical School, for the investigation of Dapanone; to the University of Utah for support of the work of M. M. Wintrobe; and to the Newark Clinical Group Research Foundation for the work of Arthur Bernstein.

**U. S. Rubber Company** has renewed its grant of a one-year graduate fellowship to assist Radcliffe College in its comprehensive management training program for women. The program is aimed at equipping women to fill executive jobs in a wide variety of industries.

## In the Laboratories

**Beckman Instruments, Inc.** has opened a large new plant in South Pasadena that will be devoted exclusively to the manufacture of synchros and associated components.

The **Du Pont Company** celebrated its 150th anniversary on July 18 with ceremonies at the site of the company's first mill on Brandywine Creek. A marker formed of one of the two millstones imported from France by the founder, for grinding the ingredients of black powder, was dedicated, and the occasion was further marked by the publication of a handsome 138-page illustrated book, *Du Pont—The Autobiography of an American Enterprise*.

**General Motors Research Laboratories** have named John M. Campbell assistant technical director. Succeding him as head of the Organic Chemistry Department is Lloyd L. Withrow.

**Gulf Research and Development Company** has named H. A. Ambrose head of its new Product Division and C. W. Montgomery head of the new Process Division. W. C. Offut will serve as assistant director. These divisions formerly comprised the Chemistry Division.

The **National Sanitation Foundation** at the University of Michigan School of Public Health will establish a new laboratory to test all equipment used in food service according to standards drawn up by industrial and public health committees from all states. A seal of approval to be issued for equipment meeting regulations will be available to manufacturers who conform to the standards. Walter D. Tiedeman, resident lecturer in environmental health, will direct the testing laboratory.

**Rayonier, Inc.**, has appointed Thomas R. Stein as resident manager of the \$25,000,000 purified wood cellulose plant under construction at Doctortown, Ga. Mr. Stein was formerly resident manager of the Minnesota and Ontario Paper Company and assistant manager in charge of engineering and construction for the Wood Conversion Company, Cloquet, Minn.

**Raytheon Manufacturing Company**, Waltham, Mass., recently dedicated a new plant that will be used by the Research Division in carrying on a major portion of the company's \$2,000,000 transistor program and for the engineering and manufacturing activities of the Equipment Divisions.

## Meetings and Elections

The **Engineering College Research Council** has named Eric A. Walker chairman and Kurt F. Wendt vice chairman for two-year terms. Elected to the council's Board of Directors were F. C. Lindvall, Raymond J. Woodrow, J. Hugh Hamilton, and T. L. Joseph.

The second **European Congress of Nobel Prize Winners**, dedicated to the winners of the Nobel Prize in chemistry, was held in Lindau im Bodensee June 23-27. Following the program of the first congress (*SCIENCE*, 115, 380 [1952]), Prince Lennart Bernadotte of Sweden was the *Ehrenprotektor* and head of a committee that included A. Zwisler, W. Frisch, Fritz Bopp, Erich Hayek, J. Speer, and G. Wittig. Otto Hahn, Frederick Soddy, Hans von Euler-Chelpin, George von Hevesy, Artturi I. Virtanen, Richard Kuhn, Hans Selye, Adolf Butenandt, Gerhard Domagk, Kurt Alder, and Irène Joliot-Curie were speakers, and Franz Karl Hein was again manager of the congress.

The annual meeting of the **Field Conference of Pennsylvania Geologists** was held at Newton, N. J., May 30-June 1. About 100 geologists from ten Eastern states attended and, in various groups, studied features of Pleistocene geology in the area, examined dikes of special petrologic interest, saw sections of Silurian and Devonian stratigraphy, visited exposures of Cambro-Ordovician and Pre-Cambrian rocks, and visited the Silurian Devonian section at Nearpass Quarries. Meredith E. Johnson, state geologist of New Jersey, was conference chairman.

New **Illuminating Engineering Society** officers for 1952-53 are: president, Everett M. Strong; vice president, Duncan M. Jones; and treasurer, Kirk M. Reid. C. C. Keller was re-elected general secretary.

An **Inter-American Society of Psychology** was formed during the International Congress of Mental Health held in Mexico City last year. The following officers were elected: president, Eduardo Krapf, University of Buenos Aires; vice president, Werner Wolff, Bard College; secretary, Oswaldo Robles, University of Mexico; treasurer, Herman Vergara, Uni-

versity of Bogota; associated vice presidents, W. Line, Canada; Enrique B. Roxo, Brazil; Carlos Nassar, Chile; and Jaime Barrios Penna, Guatemala. The Latin-American office is at the University of Mexico, and the USA office at Bard College. The first annual meeting has been planned for Caracas next December.

The **International Astrophysical Conference** will be held Sept. 19-21 at the Institut d' Astrophysique, University of Liège, and will be devoted to a discussion of "The Physics of Comets." Otto Struve will be chairman of the sessions, and the following American speakers have been announced: T. L. Page, A. McKellar and J. L. Climenhaga (Victoria, B. C.), J. Kaplan, F. L. Whipple, and G. P. Kuiper. The reports and discussions will be published by the Société Royale des Sciences de Liège.

The fourth meeting of the **International Committee of Electrochemical Thermodynamics and Kinetics** will be held in London at the Imperial Institute of Science and Technology and at Cambridge University, Sept. 10-13. Fifteen countries are represented in the membership, and in each of these a national secretary has been appointed. Proceedings of the second meeting have been published, and proceedings of the third meeting will appear shortly. For full information concerning the meeting, address Marcel Pourbaix, University of Brussels, 50 Ave. F. D. Roosevelt, Brussels, or T. P. Hoar, Department of Metallurgy, Cambridge University.

An **International Symposium on Combustion** will be held at MIT Sept. 1-5 and will be open to all those interested in the subject. Some 100 papers will be presented from Great Britain, France, Holland, Belgium, Germany, and Japan, as well as from U. S. research laboratories and educational institutions. At least 50 foreign experts in the field are expected to attend. For further information write to Hoyt C. Hottell (MIT), cochairman of the symposium.

One of the highlights of the **Midwestern Conference of Parasitologists**, holding its annual meeting at the University of Illinois June 16-17, was a panel discussion on Selected Problems in the Teaching of Parasitology. L. O. Nolf, C. A. Herriek, E. R. Becker, and W. Lindquist were participants. Dr. Herriek was elected presiding officer, and William Balamuth secretary-treasurer.

At the first regular meeting of the recently organized Washington Section of the **Society for Industrial Microbiology**, Walter N. Ezekiel was elected chairman, Paul Klens vice chairman, Charles T. Lempke, secretary-treasurer, and Carl J. Wessel assistant secretary-treasurer. An informal forum was held on the general topic of The Statistical Reliability of Present Test Procedures in the Field of Biological Deterioration, in which Dr. Wessel, Dr. Klens, Dr. Ezekiel, and Howard W. Gilbert led the discussions.

The **Wyoming Geological Association** will hold its

annual field conference Aug. 1-3 in Thermopolis. Full information may be obtained from Frank D. Helms, P. O. Box 1168, Casper, Wyo.

## Miscellaneous

**Anaconda Copper Mining Company** has elected Robert E. Dwyer president to succeed the late William H. Hoover. Edward S. McGlone was elected executive vice president, Chester H. Steel vice president in charge of Western operations, and Clyde E. Weed vice president in charge of operations of the company and its subsidiaries.

Frank B. Rogers has been appointed first director of the recently established **Armed Forces Medical Library**, largest institution of its kind in the world. Colonel Rogers had served as director of its predecessor, the Army Medical Library, since October 1949.

The Institute of International Education has named **Charles Alvin Foster** director of its European office in Paris. Dr. Foster will promote student exchange programs with many countries, will act as the institute's liaison officer with European universities, selection committees, foreign governments, and Unesco, and will counsel both American students arriving in France under the Fulbright program and French students planning to come for study to the United States.

**General Electric Company** is sponsoring a More Power to America Award—designed to "increase the productivity of American industry by encouraging creative broad-scale industrial electrification . . . and to bring recognition to the companies and individuals making the greatest advancement in this field each year." The first award will be made by the Edison Electric Institute in Chicago Apr. 1, 1953. For full information write to the institute at 420 Lexington Ave., New York 17.

The **National Geographic Society** is cosponsoring, with **Cambridge University**, the **Royal Geographical Society**, and the **Scott Polar Research Institute**, a British expedition to Spitsbergen, under the leadership of G. A. Sutton. Eight young scientists will study West Spitsbergen, largest island in the group, to gain field experience and to add to the topographical, geological, and glaciological knowledge of the area. Base camp will be at the head of Is Fjorden, on which the port of Longyearbyen is located.

The **Royal Society of Edinburgh** will award a David Anderson-Berry Prize to the person, who, in the opinion of the Council, has recently produced the best work on the therapeutical effect of x-rays on human diseases. Applications may be based on published or unpublished work and should be accompanied by copies of relevant papers. They should be in the hands of the general secretary of the society, 22 George St., Edinburgh 2, by Mar. 31, 1953.



# Technical Papers

## Disease Resistance and Early Testing of Maize<sup>1</sup>

C. C. Wernham

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The writer has been engaged in devising a program for isolating disease-resistant lines of corn since 1944. Methods and techniques used in this program have been published (1, 2). Until recently the output of resistant material was so limited as to present little difficulty in the strictly agronomic phases of yield-testing. Work conducted at this station, in addition to projects at Beltsville and Purdue, has furnished a nucleus of material of diverse origin which makes the production of large numbers of resistant inbred lines relatively easy.

Resistance to *Helminthosporium turcicum* is rare. A nursery population of 20,000 F<sub>2</sub> plants of a cross (very resistant × very susceptible) usually yields less than 20 plants of a rating 0.5-1.0 and about 40-60 plants of an acceptable rating of 2.0 (3). This selected residue yields such abundance of acceptable sublines that a major problem arises in conducting the proper experiments in yield-testing. If each original selection were represented by only two sublines in F<sub>3</sub> or F<sub>4</sub>, yield-testing is experimentally unmanageable.

The solution would appear to be early testing of the original 60 or so F<sub>2</sub> families, a number rather easily fitted into experimental design. Two arguments are presented against the procedure: (a) nonuniformity in maturity of such material makes it difficult to outcross, and (b) a second top cross at a later date is required to sort out segregates within family progenies.

In a total disease program, corn and certain maize pathogens are planted in cold wet soil. Emergence is delayed because of differentials in seedling reaction to microorganisms and/or physiological tolerance to the environment. Experience has shown that maturity dates of surviving plants from a disease nursery represent a greater spread than do similar data under normal conditions of planting. A ten-day difference in the disease nursery often shrinks to a three- or four-day difference when corn is planted in warm soil. It may well be advisable to observe the original selections for one season under normal conditions so that their functional maturity range and general agronomic characters may be observed prior to top-crossing. An alternative procedure would be to top-cross as many as fitted the pollen-shedding range of successive plantings of the male tester, and at the same time noting the maturity of those that did not fit, so that they

<sup>1</sup> Authorized for publication on Feb. 4, 1952, as paper No. 1720 in the Journal Series of the Pennsylvania Agricultural Experiment Station. Contribution No. 146 from the Botany Department, Pennsylvania State College, State College, Pa.

TABLE 1

CHANGES (ACCORDING TO GENETIC THEORY) IN COMPOSITION THROUGH FOUR GENERATIONS OF SELFING OF FIVE S<sub>0</sub> CORN PLANTS CARRYING 200 "FAVORABLE" GENE PAIRS WHICH ARE PRESENT IN EACH S<sub>0</sub> PLANT IN A DIFFERENT PROPORTION OF HOMOZYGOUS TO HETEROZYGOUS COMPOSITION

| Plant No. | S <sub>0</sub> |     | S <sub>1</sub> |    | S <sub>2</sub> |    | S <sub>3</sub> |    | S <sub>4</sub> |    | Total favorable gene pairs |
|-----------|----------------|-----|----------------|----|----------------|----|----------------|----|----------------|----|----------------------------|
|           | A*             | A†  | A              | B  | A              | B  | A              | B  | A              | B  |                            |
| 1         | 150            | 50  | 162.5‡         | 25 | 168            | 12 | 171            | 6  | 172            | 3  | 175                        |
| 2         | 100            | 100 | 225            | 50 | 137            | 25 | 143            | 12 | 146            | 6  | 152                        |
| 3         | 75             | 125 | 106            | 62 | 121            | 31 | 129            | 15 | 132            | 7  | 139                        |
| 4         | 50             | 150 | 84             | 75 | 103            | 38 | 112            | 19 | 117            | 10 | 127                        |
| 5         | 25             | 175 | 69             | 88 | 91             | 44 | 102            | 22 | 107            | 11 | 118                        |

\* A, homozygous pairs.

† B, heterozygous pairs.

‡ Hereafter figures are given in whole numbers.

could be tested the following season. In the meantime other lots of S<sub>0</sub> or F<sub>2</sub> material could be processed in the disease nursery.

The objection to an additional top-cross test at a later date (4) is not so easily disposed of. Several authors (4-7) have shown that significant segregation for yield occurs at later stages of inbreeding. All agree that the better segregates were visually undetectable. Yet all are at a loss to explain the segregation. It seems inconsistent with genetic theory.

If we consider genes for yield prepotency to have small effects, and yield-testing to be a sorting device for selecting plants with the largest blocks of favorable genes (8), the material presented in Table 1 may serve as a basis for further comment. The following postulates should be kept in mind:

a) Genetic theory requires that heterozygosity decrease by one half with each additional generation of self-pollination. The data of Jenkins (9) and Sprague (4) support this theory.

b) Half the homozygotes accumulated will be of the dominant, or plus, type, since dominants and recessives accumulate in equal numbers. (It is assumed that genes favorable for yield and vigor are of the dominant-recessive, or plus-zero, type. Therefore homozygotes will have more influence on yield of top crosses than heterozygotes.)

c) Genes in the homozygous condition may be discarded but cannot be lost by inbreeding. They can only be added to.

d) Selection practices are typical of the corn breeding procedures (i.e., a small number of ears are chosen to perpetuate each line selected and sister lines are discarded by visual evaluation).

From Table 1 it is apparent that no advantage has accrued through the accumulation of favorable genes by selfing plants 1-5. They maintain their relative position with respect to blocks of favorable genes in the homozygous condition. Although plant 5 accumu-

lates favorable genes in larger amounts, it never quite catches up (through  $S_1$  to  $S_4$ ) with plant 4, which had more favorable gene pairs in the homozygous condition to begin with.

Then if we accept, as a basis for separation, a top-cross test after  $S_3$  or  $S_4$  as a valid procedure, we must perforce assume that a similar test at  $S_0$  level is equally valid, since the different  $S_0$  plants maintain their relative positions in  $S_3$  or  $S_4$ .

The data of Sprague and Bryan (7), Payne and Hayes (6), and Lonnquist (5) clearly contradict the theory.

Segregation of genes with small effects does not seem to be an adequate answer. Ten such genes in heterozygous condition would produce 1024 possible combinations of gametes, of which 66% are in the modal classes. The distribution being normal, any random sampling of the gametes would cancel advantages or disadvantages of selection outside the mode. It is doubtful if segregation of less than ten genes (with small effects) could be detected in top crosses. There appear to be two alternate assumptions.

a) The sample size used in test-crosses is inadequate for accurate appraisal of genetic theory. The author frankly admits his academic inability to evaluate the validity of the practices in use, except to point out that general adoption of a technique does not guarantee its adequacy. Sprague and Bryan (7) present data to indicate that segregation for top-cross combining ability was not significant in 1938 but was significant for 1939 and combined 1938-39 data.

b) A relatively few genes affect yield out of all proportion to their number. In some families these occur initially in the heterozygous state, and because of their small number their genetic distribution in a nursery row of 30-35 plants is fairly common. Thus some sublines would be selected which carried these genes in the homozygous (dominant or recessive) or heterozygous state.

It is unlikely that the effect of these postulated genes is concerned with vigor; otherwise they would be discarded visually. The effect is probably more in the realm of conditioning of vital processes which affect weight and moisture content of grain. Any investigator familiar with the light chaffy ears of stalk-rotted plants could well imagine the impact of a bad stalk-rot season on the yield of susceptible top crosses (10). Sprague and Bryan (7) report segregation for lodging (erect plants) and disease resistance (kernel damage) in addition to yield differences. There is little evidence, however, of a significant positive correlation between high-yielding sublines and low lodging or few damaged kernels.

A program for the production of disease-resistant corn envisages and employs pathological techniques which sort out resistant material in a breeding nursery from the onset of the breeding program. Its purpose is not unlike, nor unrelated to, early testing for combining ability in the same lot of material. The low gene frequency of certain types of resistance demands that screening for disease reaction be carried out first.

The techniques for selecting disease-resistant corn are available. It is no more possible to select resistant corn plants without presence of disease than it is possible to select high-yielding lines without yield-testing.

There is a rapidly accumulating stockpile of resistant inbred material of a wide range of maturity which may serve as starting points in a breeding program. It is becoming increasingly apparent that native open-pollinated varieties are fertile sources of resistant material, although the gene frequency for resistance to *H. turcicum* is rather low.

Early testing for total disease is a sound program insofar as techniques are available. Segregation will occur in later generations. Early testing for yield is gaining in usage. Segregation in later generations has been demonstrated, but whether this reported segregation is permanent, as might be shown by progeny testing, or intermittent, because of unknown fluctuating environmental factors, has not been proved.

A delayed test involving  $S_1$  or  $F_3$  material is recommended for a combined program involving disease resistance. If genetic theory and the generally postulated effect of genes for yield in maize are correct, an additional top-cross test following further inbreeding is unnecessary.

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#### Chemical Constitution and Biological Activity of some Organophosphorus Compounds

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The relationship of the chemical constitution of a substance to its biological activity has been the subject of investigation since Brown and Frazer (1) attempted a generalization connecting the physiological action of a substance with its chemical structure. Many specific relationships have since been elucidated,

<sup>1</sup> Abstracted from the thesis submitted by Dasu Ramaswami in partial fulfillment of the requirements for the Ph.D. degree. D. R. is indebted to the University of Illinois for a research fellowship.

some of them (2-5) in considerable detail. These correlations are now called structure activity relationships, or SAR (3).

The concept of SAR has been used as a guide in the search for new pharmacodynamic agents.

The phosphate radical as part of the coenzymes, nucleoproteins, ATP, phospholipids, etc., plays a vital role in biological processes. A number of phosphorus compounds are highly toxic, some of them being in use as insecticides and fungicides. The phosphoryl group  $P=O$  present in all these compounds may be the factor that renders them accessible to tissue receptors or points of attachment of the enzymes these compounds may be presumed to influence. Another biologically important chemical group is the carbonyl group,  $C=O$ , present in a number of pharmacodynamic agents that are substituted carbonic esters. Such esters have examples among local anesthetics (procaine), autonomic drugs (acetylcholine, atropine), and sedatives and hypnotics (barbiturates and urethanes). The resemblance between the two groups  $P=O$  and  $C=O$

in the above compounds in regard to structure and biological importance led to the assumption that they might be mutually replaceable without loss of biological activity. This assumption has been investigated.

Phenylurethane (ethyl phenylcarbamate) has been studied for its effect on experimental animal tumors (6), as a depressant, and in inhibiting the germination of seeds selectively (7). It should be interesting if its phosphoryl analog, diethyl anilidophosphate, proves to mimic all these effects since, possibly, different physicochemical mechanisms may be involved in each effect. In a preliminary study the diethyl anilidophosphate was found to possess two of these; namely, anticonvulsant effect and growth-inhibitory effect which was, however, feeble. It may be significant that phenylurethane possesses the peptide group  $-CONH-$  present in proteins and that the analog contains the group  $-PONH-$  present in phosphocreatine.

The study was extended to the homologs of diethyl anilidophosphate, the dialkyl anilidophosphates, which

TABLE 1

| No. | Compound                       | Structural formula  | Effect on germination |           | Effect in mice—IP |            |             |
|-----|--------------------------------|---|-----------------------|-----------|-------------------|------------|-------------|
|     |                                |   | Oats                  | Charlock  | MTD (mg/kg)       | LD (mg/kg) | MED (mg/kg) |
| 1   | Phenyl urethane                | $H_3C_2O-\overset{\overset{O}{\parallel}}{C}-NH-C_6H_5$               | 4 +                   | No effect | 100               | 400        | 150         |
| *2  | Diethyl anilido phosphate      | $(H_3C_2O)_2=\overset{\overset{O}{\parallel}}{P}-NH-C_6H_5$           | 1 +                   | " "       | 100               | 666        | 533         |
| 3   | Di-n-propyl anilido phosphate  | $(n\text{-Propyl-O})_2=\overset{\overset{O}{\parallel}}{P}-NHC_6H_5$  | 3 +                   | " "       | 125               | 500        | 300         |
| *4  | Di-isopropyl anilido phosphate | $(\text{Isopropyl-O})_2=\overset{\overset{O}{\parallel}}{P}-NHC_6H_5$ | 2 +                   | " "       | 300               | 1500       | 900         |
| 5   | Di-n-butyl anilido phosphate   | $(n\text{-butyl-O})_2=\overset{\overset{O}{\parallel}}{P}-NHC_6H_5$   | 3 +                   | " "       | 100               | 400        | 300         |
| *6  | Di-isobutyl anilido phosphate  | $(\text{Isobutyl-O})_2=\overset{\overset{O}{\parallel}}{P}-NHC_6H_5$  | 2 +                   | " "       | 500               | 2000       | 1000        |
| 7   | Di-n-amyl anilido phosphate    | $(n\text{-amyl-O})_2=\overset{\overset{O}{\parallel}}{P}-NHC_6H_5$    | 2 +                   | " "       | 500               | 750        | 500         |
| 8   | Di-isoamyl anilido phosphate   | $(\text{Isoamyl-O})_2=\overset{\overset{O}{\parallel}}{P}-NHC_6H_5$   | 2 +                   | " "       | 1000              | 2000       | 1500        |
| 9   | Phenobarbital sodium           |   | Not tested            |           | 50                | 250        | 20          |

\* Compounds previously reported in the chemical literature.

1 + —Slight retardation in growth of roots and shoot.

2 + —Root growth severely retarded, slight retardation in shoot growth.

3 + —Root growth inhibited and shoot growth severely retarded.

4 + —Root and shoot growth inhibited.

MTD = Dose at which minimal toxic signs were noticed (this dose gave no protection against metrazol convulsions).

LD = Dose which killed one mouse. This is not  $LD_{50}$ .

MED = Minimal effective dose against electroshock — 0.3 sec, 15 ma; each compound was tested on a total of 18 mice.

#### Data on Germination

Oat seeds germinating, using distilled water (control)—45 out of 50.

Oat seeds germinating, using the compounds—44-48 out of 50.

Charlock seeds germinating, using distilled water (control)—23 out of 50.

Charlock seeds germinating, using the compounds—24-26 out of 50.

were synthesized and tested for the biological effects indicated by the present hypothesis. Results of the tests on mice and on the seeds of oat (*Avena sativa* L.), a monocotyledonous plant, and those of yellow charlock (*Brassica sinapis*), a dicotyledonous plant, are shown in Table 1.

In germination experiments the compounds were applied on a filter paper enclosed between two watch glasses and kept moist by a solution of a concentration of 1 g mol/million ml distilled water. The insolubility of compounds 5 to 8 called for treatment as follows: The weighed quantity was dissolved in  $\frac{1}{2}$  ml ethanol and 99 $\frac{1}{2}$  ml distilled water quickly added to the flask, which was shaken vigorously.

Results of this investigation show a broad agreement with the postulated hypothesis in regard to the anticonvulsant effect and less strikingly the selective growth-inhibitory effect. However, neither phenylurethane nor its analogs compare well in their anticonvulsant effect with phenobarbital sodium, a well-known anticonvulsant structurally unrelated to the present series. Compounds 3 and 5 are the most potent of the series, both in inhibiting germination and in anticonvulsant activity; it would be of interest to find out if they mimic the third biological effect, namely, the retardation of experimental tumors, reported to be shown by phenylurethane and isopropyl phenylcarbamate (6).

This investigation is being continued.

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## The Recording of Flight Movements in Insects<sup>1</sup>

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In studies of insect flight, wing rates have been widely used to gauge physiological activity. As these may reach frequencies of 1000/sec (1), an inexpensive, accurate, and objective recording method is not easy to find. Of the methods discussed by Chadwick (2), the stroboscopic has been the choice in several recent studies (3, 4). Where continuous records of frequency are required, a crystal pickup may be used to convert thoracic movement into electrical current (5). The discoveries of Pringle (6) and Roeder (5)

<sup>1</sup> Supported by a grant from the Graduate Research Fund of the University of Connecticut.

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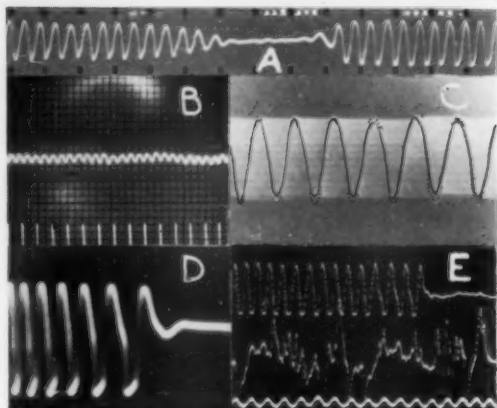


FIG. 1. A: Record of the movements of the scutellum of a fly during a stop and start; time calibration by film perforations, .014 sec. B: Electrostatic record of wing movement in a chironomid midge; time calibration, 1/300 sec. C: Superimposed simultaneous records of wing movements obtained by electrostatic method and of scutellum movements recorded by reflected light; solid line traced over cathode beam record; dotted, over light beam record. D: Record of movements of scutellum during a fast stop. E: Simultaneous records of wing movements by electrostatic method (upper trace) and of thoracic electrical activity (middle trace) during a fast stop; time calibration, 1/60 sec.

have stimulated interest in the neuromuscular mechanisms of insect flight and have made necessary the development of superior methods of recording flight movement.

With insects of reasonable size, flight movements may be recorded photokymographically with a slit camera, using a beam of light reflected from a fragment of silvered cover slip sealed to the scutellum. In flies, the movements of the scutellum reflect closely the changes in length of the indirect muscles and the movements of the wings (7). Where continuous records are required, an Army surplus GASP 16 mm gun camera can be used, provided the framing mechanism is removed and additional film guides are installed in the magazine. This gives a constant maximum film speed of 520 mm/sec, attained in 1/10 sec. Fig. 1, A is a record of movements of the scutellum in normal flight; Fig. 1, D, in a fast stop.

A more convenient method that records wing movement and may be used with the smallest insects has been developed. This depends on the fact that moving electrostatically charged bodies may act as variable condensers. The capacity charges induced by the rapidly moving, charged wings of an insect may be amplified and photographed from the screen of an oscillograph. The necessary charge is induced on the wings by the presence of a charged nonconductor. Voltages as high as 10 mv may be obtained. Even the frequency of flight movements in wingless insects has been recorded by this method. The wing frequency of untethered insects flying about in a jar may also be obtained. Fig. 1, B shows wing movements of 500/sec in a chironomid midge.



The position of the electrodes determines to some extent the nature of the record. The most accurate record of wing position is obtained if the leads are placed so that the wings move either toward or away from them. Experiments were performed to determine how closely the record gives the instantaneous wing position during a cycle. For this a simple camera was constructed in which a piece of film could be pulled past two small slits opposite each other. The antihalation back was removed from the film with hypo so that, through the slits, two simultaneous records could be made. The cathode ray and the light beam from the scutellum were superimposed through the slits, and the film was pulled past when the insect began to fly. The record (Fig. 1, C) shows almost perfect correspondence; the solid line is traced over the wing movement record and the dotted line over the scutellar movement record.

No methods of recording flight movements previously used could demonstrate the gradual development of a fast stop as shown in D, a record of scutellar movements, and E, a record obtained by the electrostatic method. The fast stop is reflected in changes in the thoracic potentials (E, middle trace). The electrostatic method, because it converts movement into electrical voltage, permits comparison with other parameters that can likewise be made to produce electrical change.

There may be some question as to whether this method records position at all movement frequencies. This can be determined directly in a specific case—at least in flies—by comparison with scutellar movements as demonstrated in this report. A simpler method of obtaining the approximate phase relation between wing position and electrical voltage is to set one input lead so that a wing just touches it when the wing is at its extreme excursion. This puts a small pip on the record at the instant the wings reverse direction. If the pip occurs at a negative or positive voltage peak, the record shows wing position. Adjustment of the polarity of the leads should be made to make a positive peak correspondence to the extreme up position and a negative peak to the extreme down position. If only wing frequency is desired these precautions are not necessary.

This method has wide application in studies of insect flight and, by comparison with the direct recording of scutellar movements, will give instantaneous position, direction of movement, and velocity during rapid flight with an accuracy sufficient for many purposes.

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## Paleobotanical Investigations in Naval Petroleum Reserve No. 4, Alaska<sup>1</sup>

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During the summer of 1951 a party from the University of Michigan spent several weeks looking for fossil plants in Naval Petroleum Reserve No. 4 in northern Alaska. The project was sponsored by the Office of Naval Research, and the Arctic Research Laboratory at Point Barrow furnished field equipment and transportation within the reserve. The party, consisting of the writer, with Richard A. Scott and J. Stewart Lowther as assistants, arrived at Point Barrow on July 3. Most of the work was done along the Colville River at the southern edge of the reserve, but a short visit was made to the coal mine at Atkasuk, about 80 miles south of Point Barrow on the Meade River. In addition to collections made by our party, one was made by W. V. Mayer at East Oumalik, which is on the northern edge of the Arctic Plateau between Point Barrow and the Colville River.

Along the Colville River, two stretches totaling about 120 miles were explored for fossil plants, using an 18-ft canvas boat for transportation. The longest of these stretches was that between the mouths of the Etivluk and Killik rivers. The rocks along this part of the Colville River belong mostly to the Nanushuk group, and the plants were found in the Chandler formation, the nonmarine part of the group which intertongues with the marine Umiat formation. Then along a shorter stretch of the river, beginning at Umiat, which is about 50 miles downstream from the mouth of the Killik River, extensive exposures within the Colville group were examined. Formerly regarded as Upper Cretaceous, the Nanushuk group is now believed by geologists who have recently worked in the reserve to be Lower Cretaceous. The Colville group has been retained in the Upper Cretaceous, where it was originally placed (1).

Fossil plants were collected at 13 localities in the Chandler formation between the places where the Etivluk and Killik rivers join the Colville. The flora of the Chandler formation is a typical late middle Mesozoic one, consisting of conifers, cycadophytes, ginkgoes, ferns, and a few fragmentary dicotyledonous leaves. The latter are always a minor element, so minor, in fact, that at the best locality none were found, although they were diligently looked for. The most abundant conifers are *Sequoia*-like forms represented by cones and foliage, and foliage of ancient members of the Taxaceae. Well-preserved silicified coniferous wood was found at several places. *Podocarpites* is very abundant, and the Ginkgoales are represented by the extinct genus *Baiera* and deeply dissected leaf-forms of *Ginkgo*. The most prevalent

<sup>1</sup>Contribution No. 1952-3 based on work done under the auspices of the Arctic Research Laboratory of the Office of Naval Research.

eycadophytes are forms resembling *Nilssonia*. A plant that is conspicuous because of the size of the leaves, but that is never present in great numbers, is a species of *Macrotaeniopteris*. Ferns are represented by *Cladophlebis* and other genera.

The Colville group is less productive of fossil plants than the Nanushuk group, although a good collection was secured from the nonmarine Prince Creek formation three miles below Gubie, near the junction of the Anaktuvuk River with the Colville. *Sequoia*-like conifers are abundant, and dicotyledonous foliage is present in larger quantities than in any of the collections from the Nanushuk group.

The fossil plants of Naval Petroleum Reserve No. 4 are of special interest because of their bearing on the age of the rock formations that contain them. Originally almost the entire mantle of sandstones and shales covering the greater part of Alaska north of the 69th parallel was believed to be of Upper Cretaceous age, and was so regarded by F. H. Knowlton, who examined several fossil plant collections secured by earlier exploring parties (2). Knowlton formulated his conclusions from the few dicotyledonous leaves in the collections. He said that since dicotyledons did not appear until middle or late Cretaceous time, the presence of even one leaf fragment would show that the rocks are not older. If dicotyledons are present, he would reject all other plants as indicators of age (2).

Knowlton's elimination of all plants except dicotyledons as age indicators was done on the assumption that these plants did not appear on the earth until mid-Cretaceous time, which of course is not true. The fact that he knew of their existence in earlier rocks is shown by his list of plants making up the Lower Cretaceous Potomac flora (3), in which there are several dicotyledons. In his exclusive use of dicotyledons for correlative purposes, and the complete disregard of all other plants that might be present, he was ignoring the essential fact that dicotyledons are sometimes present in Lower Cretaceous rocks.

In distinguishing between Upper and Lower Cretaceous on the basis of plant remains, the criterion is mainly the relative abundance of dicotyledons and other plant types. In the Upper Cretaceous of the Yukon Valley and the Alaska Peninsula, for example, dicotyledons outnumber other plants by a proportion greater than three to one. In the Dakota group, which contains the largest of known early Upper Cretaceous plant assemblages, dicotyledons make up about 90% of the flora. Other Upper Cretaceous floras show a similar high proportion of dicotyledons, although they are not necessarily as high as in the two examples given here. However, in the Nanushuk group, where dicotyledons are scarce or absent entirely, the proportion is no greater than in the lowest member of the Potomac group (the Patuxent) where dicotyledons make up an approximate 5% of the flora. If by chance one were to happen only upon those localities in the Nanushuk group where there are no dicotyledons, evidence of Jurassic age would be as strong as Creta-

ceous. In view of the few dicotyledons that are present in the group, Lower Cretaceous age practically amounts to certainty.

The plants collected from the Colville group are insufficient to characterize it definitely as either Lower or early Upper Cretaceous, but the absence there of cycadophytes and *Podozamites*, and the presence of more dicotyledons, indicate a later floral development than that revealed in the Nanushuk group.

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## Nomographs for Determining Seiche Periods

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Small variations of water level can be measured accurately; nevertheless the limnologist must still compute the theoretical seiche period. Seiches are found on all lakes but because of their small amplitude may escape notice. Seiches may be very significant in current analysis and to the ecologist. The nomographs (Figs. 1 and 2) express the seiche period in minutes or hours, and are based on Merian's formula, which was simplified by William Thompson (1). The formula is expressed as

$$t = \frac{2L}{\sqrt{gh}}$$

where  $t$  = seiche period in seconds;  $L$  = length of the center line along the seiche axis in feet;  $g$  = gravity (32.16 ft/sec/sec, 41° Lat.); and  $h$  = average depth of the basin in feet.

For an accurate computation this formula must be applied to small increments along the seiche axis (integration by approximation), but in many cases the average depth, for a small lake, will give a sufficiently accurate estimate.

A sample computation, using Fig. 1, for Lake Erie is given. The center line through the lake is 213 miles long (top line), and the average depth is 61 ft (bottom line); a line drawn between the two points shows a period of about 14.2 hr on the diagonal line, a value which agrees with computations made by Endros (2) and Olson (3).

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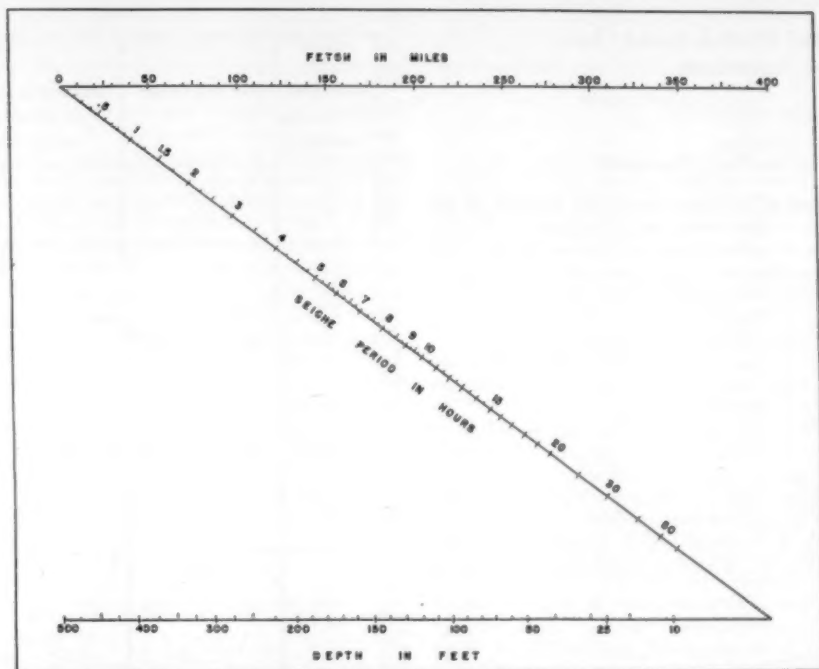


FIG. 1. Nomograph showing relationships between length, depth, and seiche period for very long or very deep lakes.

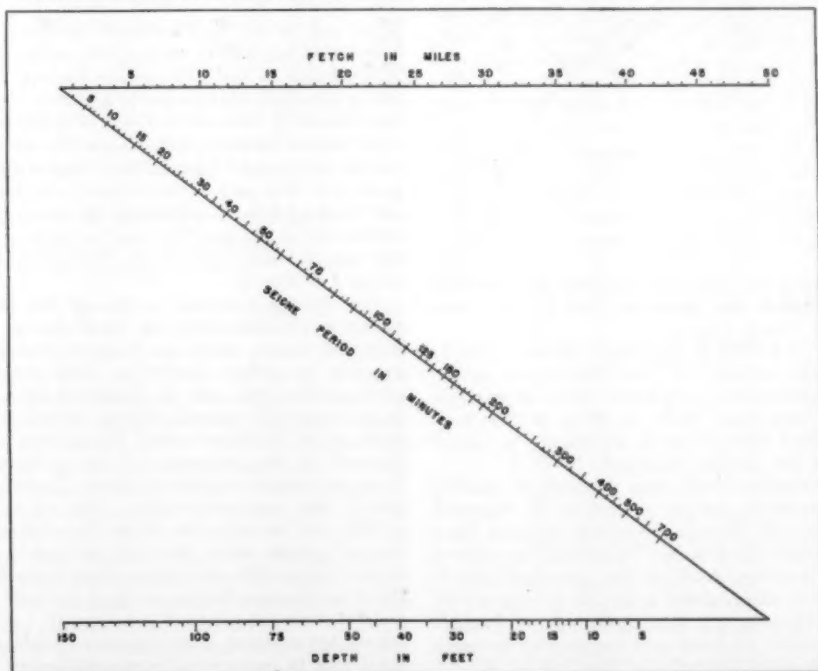


FIG. 2. Nomograph showing relationships between length, depth, and seiche period for short or shallow lakes.

# Analysis of Growth of the Chick Marginal Blastoderm

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The spread of the blastoderm over the yolk of the avian egg is being investigated in connection with the significance of yolk structure. Carbon powder and vital dye marking of the marginal cells of the blastoderm indicate that growth occurs actively from the edge and not by cell proliferation in the more proximal and central regions, with resulting passive transport of the margin. Marks placed at the edge were found to remain behind as the blastoderm continued its growth over the yolk.

The presence of free nuclei in the periblast of teleost eggs was reported by Ryder (1) and Agassiz and Whitman (2). This same situation was found to exist in pigeon eggs by Harper (3). The marginal cells of the blastoderm were found to be open peripherally, with a syncytial region extending into the periblast (Fig. 1). A more detailed study was carried

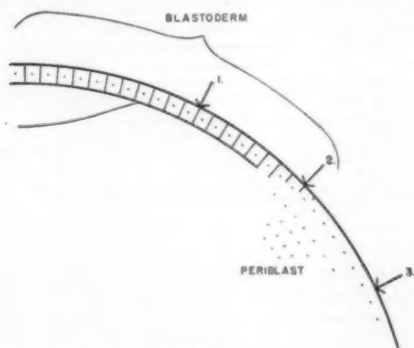


FIG. 1.

out by Blount (4), and more recently an essentially similar situation has been described for the hen's egg (5).

Blastoderm growth is considered to take place by the continual advance of these free nuclei accompanied by subsequent cytoplasmic compartmentalization. The blastoderm would, in effect, cut the marginal periblast into cells while maintaining a zone of free nuclei for further expansion.

If this situation exists, then it should be possible for the blastoderm margin to continue its migration around the yolk following complete isolation from previously established tissue. To test this, a series of isolations was performed at the sites indicated in Fig. 1. These sites, labeled 1, 2, and 3, respectively, are in the blastoderm proper, at the zone of junction where the open marginal cells merge with the peri-

<sup>1</sup>Public Health Service research fellow of the National Institutes of Health.

| AGE AT TIME<br>OF OPERATION<br>(HOURS) | SITE OF CAUTERY | APPEARANCE AFTER<br>24 HOURS OF<br>INCUBATION |
|--|-----------------|---|
| 10                                     |                 |   |
| 24                                     |                 |   |
| 24                                     |                 |   |
| 24                                     |                 |   |
| 48                                     |                 |   |

FIG. 2.

blast, and in the periblast itself. Isolation was accomplished by cautery with a fine, resistance-heated wire applied to the yolk surface through a window cut in the shell. This results in a clearly visible local coagulation of albumen and yolk that makes further identification marking unnecessary. The width of the visible injury was 1.5 mm, and vital staining with methylene blue and neotetrazolium chloride showed cell destruction for an additional 0.5 mm on both sides of the line of cautery. The windows were sealed, and the eggs incubated for 24 hr. The results are summarized in Fig. 2.

The isolated marginal portion of the blastoderm grows at approximately the same rate as the unoperated region. Since the isolated portion cannot possibly be pushed forward by more proximal cell proliferation, and since it progresses over the yolk in an apparently normal fashion, growth must take place at the blastoderm edge. This growth is not influenced by the separation of the marginal region from previously established tissue. Cauterization at site 2, the marginal region, halts all subsequent growth, and cauterization at site 3 results in a cessation of growth when the marginal cells reach the injured region. The fact that no growth of cells occurs distal to the cauterization at site 3 indicates that the isolated syncytial periblast is not capable of cell formation but evidently requires continuity with the marginal cells to undergo compartmentalization.

The growth of the isolated marginal blastoderm has

been described in *Fundulus* eggs by Trinkaus (6). Removal of the blastocoel roof in this form has no effect upon further epiboly of the remaining peripheral portion of the blastoderm. Trinkaus has provided evidence for the role of the contractile tension developed by the surface gel layer which "pulls the blastoderm down over the yolk." The operation of a similar mechanism in the hen's egg is doubtful in view of the following observations. Small defects created in the path of the advancing blastoderm demonstrate that growth is not limited to one direction. In addition to downward spread, the blastoderm, after bypassing the defect, is capable of both lateral and upward growth. Furthermore, since cauterization at site 3 does not cause an immediate cessation of growth (as would be expected if contractile tension were pulling the blastoderm down) and, furthermore, has no effect upon growth until the blastoderm margin actually touches the damaged region, it is clear that contractile tension does not influence blastodermal growth in the hen's egg. Recent evidence (7) indicates that the role of the surface contractile tension in *Fundulus* epiboly is not a major one.

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### On the Nature of the So-Called Background Material in Estrogen Fractions of Extracts Prepared from Hydrolyzed Urine<sup>1</sup>

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In 1948 Friedgood, Garst, and Haagen-Smit (1) reported an essentially new micromethod for the extraction and partition of crystalline estrone, estradiol, and estriol, and for their quantitative assay by ultraviolet spectrophotometry. In the course of applying this method to the extraction of the natural estrogens from hydrolyzed urine, to their subsequent separation from urinary phenols and neutral steroids, and to their partition from one another, it was found that the so-called background material (2-8) interfered significantly (9-11).

We have tried various methods for the separation of the "background" material from the urinary estrogens: as, for example, modification of the procedure for the steam distillation of the phenolic fraction, various washes of the extracts, changes in the solvents for

<sup>1</sup>These studies were supported by a generous grant from the California Institute for Cancer Research, Los Angeles.

TABLE 1  
FUNDAMENTAL ANALYSIS OF STEROIDLIKE MATERIAL:  
COMPARISON WITH VALUES FOR THEORETICAL  
ESTRIOL DERIVATIVES

|                              | Carbon<br>(%) | Hydrogen<br>(%) |
|------------------------------|---------------|-----------------|
| Steroidlike material         | 71.5          | 7.6             |
| Theoretical estriol catechol | 71.1          | 7.9             |
| Theoretical estriol quinone  | 71.6          | 7.3             |

equilibration, and variations of the pH at which the extractions were done. Although some of these attempts produced considerable reduction in the amount of the interfering ultraviolet-absorbing material in the final extracts, some interference persisted. At that point in the investigation a number of observations from a variety of experiments indicated that the "background" material might consist of a phenolic steroid or steroids which developed a quinone structure during the extraction procedure. A fundamental analysis done on a partially purified sample lent further support to this interpretation of the data (Table 1). A large part of this steroidlike mixture has been found to exhibit physical and chemical properties similar to those of estriol when studied in the Craig distributor and by rubber chromatography according to the method of Nyc, Maron, Garst, and Friedgood (12). Moreover, comparison of the ultraviolet spectrum of this steroidlike material with that of a synthetic estrogen derivative (13) indicates a possible structural relationship of the steroidlike material to the natural estrogens (Fig. 1).

This steroidlike material is found consistently in the urine of both males and females; and it is increased in amount about threefold during pregnancy. The excretion values in nonpregnancy urines are rather constant; they are of the order of 3-4 mg/24-hr sample.

A further study of this steroidlike material is now in progress in order to achieve its complete identification, as well as its separation from the natural urinary estrogens.

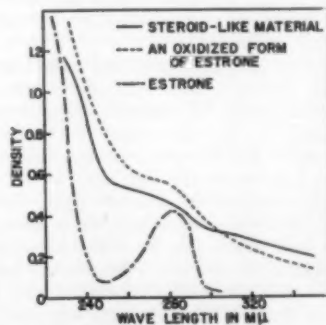


FIG. 1. Comparison of the ultraviolet absorption of the steroidlike material with that of an oxidized form of estrone. The latter was produced by exposing a mixture of estrone and 10% of its weight of riboflavin to 100 ft-c of light for 3 days.

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## Inbred Strains of *Culex* Mosquitoes

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Many studies are in progress using mosquitoes as laboratory animals, some of the most prominent of which are studies of various insecticides and the resistance of mosquito strains to them. The results of these experiments have varied widely for a number of reasons. One important source of the varying results can probably be found in the inherent genetic differences in the stocks used.

The genetic experiments using *Culex* mosquitoes in this laboratory have indicated that wild-caught strains of *Culex pipiens* and *C. quinquefasciatus* vary widely in many respects. Ordinary laboratory-bred strains also show a wide range of expression of phenotypic characteristics. In the course of our experiments it has been necessary to develop inbred strains of these two species, with the ultimate aim of as high a degree of homozygosity as possible.

One stock of *C. quinquefasciatus* maintained in this laboratory was originally obtained from Don W. Micks at Galveston, Texas, and had been maintained by him for several generations as a laboratory stock. A wild-caught strain of *C. pipiens*, from Champaign, Ill., is at present in use.

These stocks have been carefully inbred according to the plan described below. All stocks were begun from single egg rafts. The larvae from each raft were raised separately, and the pupae transferred to a new cage. Males and females from the same egg raft were allowed to mate, the egg rafts were collected, and the larvae raised in separate pans. From this  $F_1$ , one egg raft was selected, the adults were allowed to emerge and mate, and  $F_2$  rafts collected. Thus each generation is the result of brother-and-sister mating, and each succeeding generation ( $F_1$ ,  $F_2$ ,  $F_3$ ,  $F_4$ , etc.) is derived from a single egg raft, raised in a new cage. There is no backcrossing and no outcrossing, even to members of the same original stock, and thus the inbreeding is as strict as possible in animals with bisexual reproduction.

The *C. quinquefasciatus* stock is at present in the  $F_{20}$  generation, and the *C. pipiens* stock in the  $F_{12}$ . Following the method given by Wright (1) the *pipiens* stock in the  $F_{12}$  is calculated to be more than 95% homozygous, and the *quinquefasciatus* in the  $F_{20}$  should be about 99% homozygous. Sixteen generations of brother-sister matings will result in about 98% homozygosity. By way of contrast, one technique commonly used in mass cultures of these mosquitoes has been to isolate all  $F_1$  rafts, then isolate the  $F_2$ , and so forth. This method is little more than random mating and, assuming that other factors (mutation, selection, etc.) are negligible, the population should be just as heterozygous in the  $n$ th generation as it was in the first. It is therefore possible that many laboratory colonies, as well as wild-caught strains, have considerably different genetic backgrounds. Other characteristics of these stocks, defined in terms of the biological properties which they possess are as follows:

### *C. pipiens*

a) Stenogamic: Mating and egg deposition take place in cages  $30 \times 30 \times 30$  cm. Although most strains of *C. pipiens* (not *molestus* or *autogenicus*) are eurygamic, we have never experienced any difficulty in getting this strain to mate in cages of this size. If, of course, eurygamy is defined on the basis of mating on the wing rather than on the basis of cage size, the term is a matter of definition. This strain has never been observed to mate at rest, but will mate in flight. It is a striking coincidence that of several strains of *C. pipiens* which have been collected in the vicinity of Champaign, none has ever been found which would not breed in cages of this size if other rearing conditions were right.

b) Anautogenous: A blood meal is required before egg deposition. As far as we know, we have never had an autogenous egg raft. Repeated isolations of males and females, supplied with water, moistened prunes, raisins, apple slices, or sugar solutions, have never resulted in a single egg raft. On the other hand, egg deposition has always been associated with a previous blood meal.

c) Ornithophily: Although this strain will bite man—infrequently, and only when no bird blood is available—its definite preference is for birds. We normally use pigeons, but the strain has also fed on chickens. Individual females seem to differ in their biting habits. Some will avidly feed on the pigeon no matter at what time it is introduced into the cage; others prefer to feed in the evening.

d) Modified heterodynamy: Heterodynamy is a term which has been applied to those strains which undergo a diapause, or temporary cessation of reproductive function, especially during the winter months. Few laboratories have succeeded in rearing *C. pipiens* on a year-round basis, owing principally to this factor. Our strain seems to possess the genetic basis for this character, but its manifestation is modified, we believe, by the use of continuous light in the

insectary during the winter months. Without light 24 hr a day, the females will (1) not feed, (2) refuse to lay eggs, or (3) lay infertile eggs.

In continuous electric light and favorable laboratory conditions, fertilization and the deposition of fertile eggs do take place, although at a noticeably slower rate than in the summer. The reduced fertility is also marked in comparison with the behavior of *C. quinquefasciatus*, which in our stocks, at least, does not seem to possess this characteristic.

#### *Culex quinquefasciatus*

Three stocks of this species are currently maintained. One is the Galveston, Texas, stock described above. A second originated from a single egg raft from Bakersfield, Calif., obtained through the courtesy of R. E. Bellamy and Lewis W. Isaak. The third was obtained from Albert Miller at Tulane Univer-

sity. As far as we can tell, these three stocks are exactly alike in their biological characteristics. All breed readily in cages 30 x 30 x 30 cm and are therefore stenogamic. All three require a blood meal before egg deposition, and are hence anautogenous. They feed avidly on both pigeons and chickens, at almost any time of the day, as well as at night. The Galveston strain will bite man reluctantly; the other two have not been tested in this regard. As noted above, none of these strains shows any evidence of a seasonal pause in reproductive activity.

The stocks maintained in this laboratory, therefore, might be of use in various types of experiments in which stabilization of the genetic background of the strain is desirable.

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## Comments and Communications

### Vitality of the Aged

C. H. FORSYTH has presented a note (*SCIENCE*, 115, 251 [1952]) indicating that in contrast with the conclusions of his earlier study (*SCIENCE*, 70, 85 [1929]) mortality of the aged now seems to be improving. He concludes that, from 1890 on, mortality increased and reached a maximum between 1910 and 1920 and, since then, has been improving (i.e., rates have been decreasing).

Forsyth's data are for seven selected states and do not extend beyond 1940. Actual analysis for the entire United States is now possible for the last two decades. During the 1940s there was a rather astounding improvement; this will be definitely indicated when the official life tables based on the 1950 census and vital statistics for 1949-51 are available.

Table 1 gives death rates comparable to Forsyth's, based on official life tables from 1900 through 1940, with the 1948 data developed from official abridged tables. The fact that there are different areas covered in the various years can be taken into account since data for all areas are available for 1929-31 and can be compared. The table shows no evidence of significant changes in mortality of the aged from 1900 through 1930. The low rate for 1919-21 is not especially significant because, as has been pointed out in many places, this was related to the high influenza mortality of 1918, which removed rather prematurely the somewhat impaired lives. Differences in rates in the years before 1930 appear to be due mainly to statistical fluctuations; it should be recognized in any event that mortality rates for ages 70 and over, especially in small population groups such as Forsyth dealt with, are not too reliable because of the relatively small numbers involved, not to mention errors in reporting.

Since 1930, there seems to have been a definite improvement for all categories, and especially for women. The mortality rates for 1948 are well below those for the early part of the century and apparently by much greater amounts than can be attributed to random fluctuations. Data for years between 1940 and 1948 have also been analyzed and show the same general trend.

The earlier Forsyth article draws some conclusions that, in retrospect, seem rather surprising. Forsyth then concluded that "the whole picture, from our earliest records in 1890 to the present time, points constantly and inevitably to a future declining average length of life until the American adult wakes up to the fact that the odds are at present heavily against his living as long as his father or grandfather." Further, he states that the decline in longevity at advanced ages "already dominates and the average length of life—or at least the expectation from age ten—is already going down."

Table 2 shows the opposite to be true. The expectation at age 20 has risen steadily and significantly throughout the entire period for both men and women, and the increase over the past half-century amounts to about 15% for men and 20% for women. The expectations for men aged 50 and 70, and for women aged 70 remained more or less constant over the first 30 years of this century, but since 1930 have risen definitely and significantly. The expectation for women aged 50 increased slowly during the first 30 years of the century and more rapidly thereafter.

This analysis corroborates Forsyth's conclusion that mortality among the aged has improved since about 1915—in fact, later data strengthen his conclusion. However, the statistical evidence indicates that there was no significant worsening of mortality among the



TABLE 1  
U. S. DEATH RATES (Per 10,000)

| Year    | Area                         | White male |        | White female |        |
|---------|------------------------------|------------|--------|--------------|--------|
|         |                              | Age 70     | Age 80 | Age 70       | Age 80 |
| 1900-02 | Original registration states | 589        | 1335   | 537          | 1211   |
| 1909-11 | " " "                        | 621        | 1358   | 566          | 1258   |
| 1919-21 | Registration states of 1920  | 546        | 1197   | 502          | 1134   |
| 1929-31 | Original registration states | 609        | 1336   | 520          | 1210   |
| 1929-31 | Registration states of 1920  | 585        | 1298   | 492          | 1173   |
| 1929-31 | Total United States          | 580        | 1300   | 487          | 1174   |
| 1939-41 | " " "                        | 545        | 1247   | 423          | 1082   |
| 1948    | " " "                        | 532        | 1107   | 367          | 995    |

TABLE 2  
LIFE EXPECTANCY (U. S.)

| Year    | Area                         | White male |        |        | White female |        |        |
|---------|------------------------------|------------|--------|--------|--------------|--------|--------|
|         |                              | Age 20     | Age 50 | Age 70 | Age 20       | Age 50 | Age 70 |
| 1900-02 | Original registration states | 42.19      | 20.76  | 9.03   | 43.77        | 21.89  | 9.59   |
| 1909-11 | " " "                        | 42.71      | 20.39  | 8.83   | 44.88        | 21.74  | 9.38   |
| 1919-21 | Registration states of 1920  | 45.69      | 22.22  | 9.51   | 46.46        | 23.12  | 9.94   |
| 1929-31 | Original registration states | 45.50      | 20.84  | 8.95   | 47.96        | 22.69  | 9.69   |
| 1929-31 | Registration states of 1920  | 45.92      | 21.39  | 9.17   | 48.47        | 23.29  | 9.93   |
| 1929-31 | Total United States          | 46.02      | 21.51  | 9.20   | 48.52        | 23.41  | 9.98   |
| 1939-41 | " " "                        | 47.76      | 21.96  | 9.42   | 51.38        | 24.72  | 10.50  |
| 1948    | " " "                        | 48.97      | 22.44  | 9.76   | 53.80        | 26.16  | 11.17  |

aged during the early part of the century, but rather that the changes shown reflect accidental fluctuations rather than any long-term trend. Moreover, the data presented show that Forsyth's pessimistic 1929 conclusions as to a long-term decline in the average length

of life for adults were as much in error as some of the rosy economic predictions also made then.

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## Science and Technology in Unesco

THE NRC Committee on Unesco was asked to participate in the program planning and execution for the Third National Conference of the U. S. National Commission for Unesco on Jan. 27-30, 1952. J. S. Nicholas was asked to be chairman of the scientists and engineers panel, and M. B. Visscher was asked to be the discussion leader for Work Group 9, which comprised the scientists and engineers. A document was prepared comprising the conclusions and recommendations of this work group on the topic assigned—namely, "The Opportunity for Scientists and Engineers to Contribute to Peace Through the United Nations System."

There was an attendance of approximately 100 scientists and engineers at the meeting that developed this document, and the precise statements were approved unanimously by the members of the work group before they were accepted for inclusion in the attached statement. This fact is of some importance, because it indicates that it was possible to obtain unanimity of opinion with regard to several very basic questions. The supplementary Work Group 9 report by the Engineers Joint Council was prepared

by the engineers subcommittee of the work group and is referred to in Item 7 of the main report.

MAURICE B. VISSCHER

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### Third National Conference

United States National Commission for UNESCO  
Work Group 9

The Opportunities for Scientists and Engineers to  
Contribute to Peace through the United  
Nations System

The conclusions and recommendations were formulated by representatives of the basic sciences, various fields of applied science, including the engineering sciences:

1. *The Place of Science and Technology in UNESCO.* Science and technology are by custom and historical tradition international cooperative enterprises. The scientific method is universal; accordingly, no group or nation can claim unique interest in it. The results of scientific study are of immediate or potential value to all nations. The promotion of science for its own sake is not the prime objective of UNESCO; however, the chartered objective of UNESCO cannot be achieved without encouraging or

promoting both basic and applied science as a means to the ultimate end.

2. *The Future Program for Science in UNESCO.* The work group is disturbed about the fact that there is so little reference to the scientific and technological program of UNESCO in the report of the program committee of the National Commission for 1953-54. The group trusts that the U. S. National Commission recognizes the past achievements and the important role of UNESCO's work in the basic and applied sciences and requests the U. S. National Commission to urge that there be no reduction in the limited funds now allotted for the key items of the present UNESCO science program; notably:

- a. technical assistance and the field sciences cooperation offices.
- b. grants in aid.
- c. international research laboratories.
- d. documentation and scientific abstracting.

We note with interest and approval that the report of the program committee stresses the importance of increased emphasis and the possible change of direction in the areas of the social implications in science.

3. *Barriers to Exchange of Information and Travel.* Unnecessary and undesirable restrictions on exchange of information and travel of scientists exist in certain countries, including the U.S.A. Free exchange of information and facilitation of travel are both essential to scientific progress and human welfare. Any unnecessary restrictions are harmful to the advance of science and to promotion of international understanding and are consequently detrimental to the cause of peace. There is particularly the unfortunate fact that such impediments exist in this country.

4. *Evaluation of UNESCO's Grant-in-Aid Program.* UNESCO's program has consisted of joint support with organizations of scientists and engineers of international cooperative projects which either require international action or are of great importance to many national groups. The grants made have proved effective in facilitating international cooperation of scientists and engineers. The working group recognizes that we face continuing problems of evaluation, and that a balance must be struck between basic and applied science as regards magnitude of support within a limited UNESCO budget. . . . The assistance to medical and engineering sciences must be brought up to the level of support for the more basic sciences. This working group believes that attention should be given to the promotion of international cooperation in the agricultural sciences, if possible in cooperation with FAO. These additional activities should be supported without diminution in subsidy to the basic sciences.

5. *Evaluation of International Research Laboratories.* The group commends the way in which UNESCO is aiding in planning and encouraging the establishment of the first International Research Laboratories. It is believed that the International Computation Center should be put in operation promptly.

6. *The Promotion of Cooperation in Research in Major Area Problems.* The working group commends the effects of UNESCO to engage in research, particularly "to improve the living conditions of mankind." . . . This must include improved food production, better utilization of minerals, metals, and other natural resources, wider use of technical skills, and improvements in public health. In the phase of food production the Arid Zone Research Council appears to be operating effectively. This council may well serve as a model for activities in other fields.

Attention was called to the urgent need for international cooperation in the development of newer methods for the finding and utilization of mineral resources. The known world's reserves of numerous essential metals would be exhausted inside of 25 years if the per capita use of metals in the rest of the world equalled that in the U. S. In the view of the current U. N. program to raise the world living standard, attention is called to the dependence of the American living standard on metals and minerals. We recommend the formation of a research council to consider the mineral resources problem on a world basis.

7. *Better Utilisation of the Services of Engineers.* It is the feeling of this body that the services of the engineering profession have not been adequately utilized in the program of UNESCO. It is urgent, therefore, that the EJC be invited to submit proposals with a view to utilization and services in the broadest possible ways in the future activities of UNESCO. There is appended hereto an initial survey of proposals that should be transmitted to the secretary of the National Commission.

8. *Evaluation of UNESCO's Program in Scientific Abstracting and Indexing.* The work of the past four years in this field is generally approved. It is noted with regret that the U. S. National Commission has not followed through the recommendations of the conference on Science Abstracting in its final act, particularly in connection with the setting up of working groups within this country for the abstracting and indexing of scientific literature in the interest of better utilization of discoveries in the promotion of the aims of UNESCO. Further intensive study of the problems involved in effective abstracting and indexing is recommended, including consideration of possible new techniques.

9. *The Trend Toward Increasing Isolation in Science in the U. S.* Studies of literature citations in scientific publications in the U. S. show an increased trend to mention only U. S. research reports. Ignorance of foreign literature leads to wasteful duplication of work, slowing up the progress of science, and failure to utilize discoveries for useful practical purposes. Scientific nationalism, even when due to ignorance, leads to international misunderstanding; hence the correction of this trend is important to the promotion of international amity. Therefore this problem is of concern to UNESCO.

There are two important fields in which this can be specially implemented:

a. through more efficient abstracting and indexing services on an international level, and

b. by calling this question to the attention of college and university teachers.

10. We, as scientists, recognize the need for facilitation of freedom of movement of goods and services in the development of resources in the interests of world tranquillity. We feel that the example of the U. S. government has not been, and is not now, encouraging in this respect. We particularly deplore the imposition of barriers of all kinds other than those which have a sound biological basis for conserving the natural resources of member nations.

11. *Resources and Populations.* The natural sciences working party has emphasized the importance of improved food production, of thorough consideration of the importance of minerals and metals, and of the need for relative freedom of exchange of goods and services in improving the living conditions of mankind.

We recognize also the importance of population in relation to resources and urge that this problem be clearly

recognized and given serious consideration by UNESCO.

12. *Interdisciplinary Conferences.* This group notes with approval the interdisciplinary conferences sponsored by UNESCO and recommends their continuation and expansion. These serve the important end of bridging the gulfs and prejudices between scientific disciplines which have led to overdepartmentalization in academic research bodies and have seriously retarded the advance of scientific knowledge.

#### Engineers Joint Council

##### *Supplementary Work Group 9 Report*

Close cooperation between UNESCO and the world-wide engineering profession and between the engineering societies and other agencies concerned with international relations should encourage practical extension of UNESCO's immediate and long-range activities. In this connection, the Engineers Joint Council's International Relations Committee has a Commission on Technical Assistance for the following primary purposes:

A. To establish and maintain liaison with such organizations as the Economic and Social Council and other U. N. agencies concerned with international technical assistance, the U. S. Department of State (in its administration of Point IV and related operations), the Mutual Security Agency, and the Anglo-American Council of Productivity so that information or requests for advice or aid from these organizations may be promptly channeled to the appropriate group or individuals.

B. To give direction to any other activities that the Engineers Joint Council may decide to undertake in the field of engineering assistance.

Also EJC has close contact with the National Management Council, which is the U. S. Member of the International Committee of Scientific Management and is collaborating with the Mutual Security Agency in advancing scientific management in Europe. Another noteworthy citation is the establishment of cooperative relations with Latin American engineers through the creation of the Pan American Union of Engineering Societies. Furthermore, EJC, through association with the International Relations Committee of the American Society for Engineering Education, maintains an exchange of ideas, information, and personnel in engineering education. In these ways the engineering profession in the United States is being brought into intimate contact and effective relationship with engineers throughout the world.

To be most effective, it is felt that:

A. In the selection of engineering personnel for foreign service, the advice of the major professional organizations should be sought and utilized. These engineering institutes and societies constitute an already existing facility for the primary selection of possible candidates for such employment.

B. For preliminary surveys of industrial projects both government and independent engineers should be used; but for the carrying out of the projects, private engineering firms which specialize in the work involved should be engaged and the projects completed by private enterprise.

It is believed further that initiation, encouragement, and support should be given to:

1. Education in the engineering sciences of selected qualified foreign students to be sent to the United States from underdeveloped and other foreign countries.

2. Programs of assistance in developing engineering education in foreign countries.

In order to be of greatest service in utilizing and shar-

ing their special knowledge, the engineering profession could benefit from UNESCO's aid in determining:

1. Needs to be met.

2. General and technical knowledge and personality traits desirable in engineers who are to participate. For example, the latter attitudes, characteristics, and behavior tendencies may be exhibited by the individual's cultural background, sympathy, humility, and adjustability to the environment.

3. Manpower resources available for participation in projects.

4. Engineering programs planned on a world-wide basis so that future demands for engineering skills can be anticipated. This will reveal the time available for the training of engineering personnel.

To this cooperative effort The Engineers Joint Council, with its Committee on International Relations and its Commission on Technical Assistance, is dedicated in its objective to advance the general welfare of mankind through the available resources and creative ability of the engineering profession.

## Perpetual Motion and Perpetual Research

If I were concerned with sociology, I would agree with Leaver and Brown (*SCIENCE*, 114, 379 [1951]) that general laws are not unwanted in the field of social science. I would not, however, prove this point by making reference to the frustrations of those who sought perpetual motion machines before the law of conservation of energy was known, because recognition of this fundamental law would have been much delayed (historically) had not such research occurred. Clearly this was not altogether wasted effort, nor should it be implied that the efforts of social scientists today, who drift around (and sometimes sink) in uncharted waters without a compass, are without reward.

As a youth it was my fate to have encouragement from teachers to follow a not-uncommon inclination where problems are resolved by considering basic postulates without reference to earlier, more classical solutions. I must confess that I spent an enormous amount of time on projects such as the design of perpetual motion machines and the trisection of the angle by rule and compass. Is it to be inferred that there are some who categorically reject this theory of education?

I conclude that Leaver and Brown are among those who wish very much they could be alive a thousand years from now, to marvel at and to enjoy the supposed progress which will mark civilization at that far distant time. However, there seems to be no justification of existence if it is not asserted that today is a better time than tomorrow to live.

It does not seem to be a serious matter how soon the social science law of energy conservation is discovered, as long as thinkers can be delighted and excited by thoughts of social science perpetual motion machines.

WALTER ROSE

The Oil and Gas Journal  
Houston, Texas

Mr. LEAVER and I would be the last to deny that today is a good era in which to live. We are having a wonderful time and, although we notice one or two imperfections in our society, we would certainly not take any bets that society would be better a thousand years hence. Far from believing in automatic progress, I think it is at least implied in our paper that we belong to the school of thought which feels that the natural course of development is toward dissolution and decay.

I am no expert on the history of invention, but it does seem clear to me, at least from reading the

transactions of the Philosophical Society for a period covering the first half of the eighteenth century, that an immense amount of effort was wasted on the development of perpetual motion machines. Similarly, vast numbers of man-hours were wasted on the same project even after the possibility of attaining perpetual motion had been definitely disproved. This was done by those thousands of people (among them Mr. Rose) who had not yet got around to reading the literature on the subject.

J. J. BROWN

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## Book Reviews

**Die Sonnenkorona: Beobachtungen der Korona 1939-1949**, Vol. I. M. Waldmeier. Basel: Verlag Birkhäuser, 1951. 270 pp. Sw. fr. 24.60; cloth, Sw. fr. 28.60.

At present the investigation of the solar corona can be considered as the central problem of solar research. Since 1931, when B. Lyot succeeded in constructing a coronagraph, which permits regular observation and photography of the corona independent of the event of a solar eclipse, considerable advance has been made in the understanding of this phenomenon. This rapid progress is vividly illustrated by the fact that the present comprehensive treatment of corona physics could be undertaken just two decades later. The author, an authority in this field of research, is director of the Swiss Federal Observatory in Zurich. For decades the scientific program there has been devoted to solar research and, as a result of Waldmeier's efforts, the observatory has extended its activities to corona research. For this purpose, a special observatory has been established on a mountain near Arosa at an altitude of 6725 feet, and extensive research has been carried out since 1939. By means of spectroscopic investigations with a coronagraph, the intensities of two corona lines have been measured as a function of the position angle of the solar disk. The two corona lines employed are the green and red, with wavelengths of 5303 and 6374 Å, respectively, attributed by Grotrian and Edlén to forbidden transitions in highly ionized states of the iron atom, namely, Fe XIV and Fe X.

The present volume contains a detailed description of the observatory in Arosa, the coronagraph, and the spectroscopic equipment. After a discussion of the research program and a description of the method employed, there are 1410 polar diagrams containing the spectrophotometric observations made with the green and red corona lines. The statistical evaluation of this extensive material will be given in a second volume, which will also contain results of further investigations. A third volume is planned to present a comprehensive treatment of our knowledge of corona

physics. All scientists interested in this fascinating subject look forward with great expectation to the publication of these volumes.

It may be mentioned that at present five observatories are active in this type of research. Besides the original one of B. Lyot on the Pic du Midi in France, there are others in Austria, Germany, Switzerland, and the United States (at Climax, Colorado).

K. W. MEISSNER

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**Organic Chemistry** (Holleman's). Rev. by J. P. Wibaut; trans. from 16th Dutch ed. by Samuel Coffey. Houston-Amsterdam: Elsevier, 1951. 660 pp. \$9.00.

To one who some 25 years ago was nourished on Holleman's *Organic Chemistry*, this revision and modernization by Professor Wibaut is most welcome. It has always seemed a glaring omission that some qualified person had not undertaken a definitive revision of what was in its prime one of the classics of elementary organic chemistry textbooks. It was, therefore, with considerable anticipation that this reviewer began perusal of the latest edition of Holleman.

It must be admitted, however, that the reader's hopes were somewhat dampened. It developed that the thickness of the paper on which the book is printed had contributed strongly to the visions he had entertained regarding the comprehensiveness of the revised Holleman.

As stated in the preface, the book is intended not only for students who have chosen chemistry as their main subject, but also for students of medicine and biology. In the attainment of this aim Wibaut has succeeded admirably. The ultramodern organic chemist, who can find no basis for the subject other than in indiscriminate use of ionic conceptions, will undoubtedly find much to criticize in this edition. On the other hand, those who cling to the classical approach to the subject, tempered with a modest introduction of the newer concepts, will find much comfort in the presentation of the material. In the opinion of this reviewer, Wibaut has succeeded admirably in blending the old



and the new in such fashion as to provide an excellent basis for the student who desires some knowledge of organic chemistry—either as a subsidiary discipline or as a basis for further delving into its details.

Noteworthy are the discussions of recent advances in the chemistry of acetylenes, cyclo-octatetraene, the use of isotopes in elucidation of reaction mechanisms, and the introduction of modern ideas on biochemistry.

It is a pleasure to commend the present volume as an excellent introduction to organic chemistry without commitment that the book pretends to be more than its author sets forth in the preface.

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***The Geography of Europe.*** 2nd ed. George D. Hubbard. New York: Appleton-Century-Crofts, 1952. 870 pp. \$6.75.

Geographers and others interested in Europe will welcome the appearance of a revised edition of this well-known textbook. The author is professor emeritus of geology and geography from Oberlin College—a vigorous little man with a gray goatee, a twinkle in his eye, and a question on his lips, who looks for all the world like an elderly teacher from a centuries-old university in one of the countries he is describing. Professor Hubbard is a geographer of the old school who does not hesitate to employ a geologic term or refer to a geologic period when he feels it will improve his description or his interpretation. For such boldness this reviewer would like to commend him.

Approximately one sixth of the 800-odd pages in the book are devoted to aspects of Europe as a whole, and the remaining five sixths to a presentation of individual countries grouped for convenience on a broad basis of climatic similarity. Anthropogeography gets more than the customary attention, with a good chapter on the "Geography of Prehistoric Men in Europe," and a closing section entitled "Geography in the Fourth Dimension," which includes well-written chapters on agriculture, commerce, and culture.

*The Geography of Europe* is not a book to which one can turn for a completely up-to-date treatment of the European economy. Production figures and ratios have been reduced somewhat beyond the desirable minimum, but perhaps the author feels that such ephemeral facts can best be left to the annually revised statistical yearbooks. The book does provide, however, a good introduction to the broader physical and human patterns of the continent and can safely be recommended to both the student and the general reader. Most of the black-and-white maps are well selected, and a welcome addition to the revision is a colored political map with shaded relief, inside the front cover. More maps of the entire continent, showing, for instance, population distribution, agricultural regions, and coal basins, would certainly be desirable additions in a future revision. Many new pictures have been incorporated in the 1952 edition, and the bibliographies have been completely redone. As in the first edition, too many inconsequential books are cited and

too little of the available periodical literature. The author makes passing mention of the *Géographie Universelle* series in his bibliographies but fails to credit De Martonne and Demangeon with authorship of the three final volumes on France. It seems doubtful that he has consulted much of the European literature on the continent he is describing.

RALPH E. OLSON

Department of Geography, University of Oklahoma

***The Chemistry of Lignin.*** Friedrich Emil Brauns. New York: Academic Press, 1952. 808 pp. \$14.50.

This monograph is a comprehensive treatise on the chemistry of lignin and should be considered a valuable addition to the library of the plant biochemist, the organic chemist interested in natural products, the plant physiologist, and others whose work or interests are associated with the chemical aspects of wood technology and utilization.

After a brief introduction to the nature and scope of the problems of lignin chemistry and the evolutionary development of research in the field, since its first recognition as a plant constituent, the author sets about to define lignin according to the present knowledge; to outline its distribution in the plant kingdom; and to discuss its morphological relationship to the plant tissue in which it occurs. Theories on the biosynthesis of lignin are reserved for discussion in a later chapter.

The chemistry of lignin is presented in an orderly progression from detailed discussion and evaluation of the methods for its isolation and determination to a broad but detailed outline of its physical properties and chemical reactions with organic and inorganic reagents—concluding with a consideration of the numerous theories on its chemical structure and relationship to other constituents of the plant cell wall. A brief account is given of attempts to synthesize lignin, and a short appendix of laboratory techniques is included.

Throughout the writing an intensive effort is apparent to establish a rational nomenclature for the multitude of lignin preparations and reaction products which appear in the literature, and to suggest methods of oriented approach to the great variety of problems which confront present and future workers in the field.

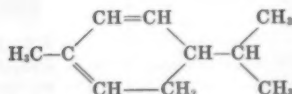
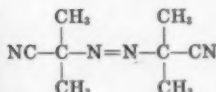
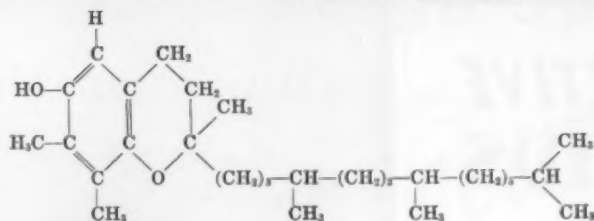
Literature citation is comprehensive although some readers may feel that significant papers have been excluded—a situation which the reviewer feels may be due to the extreme diversity of opinion and experimentation in the field. In general, the author has adhered to his stated intention of offering objective comment and interpretation where conflicting results are compared, and the book will serve as a much-needed blending medium to the vast and heterogeneous range of investigations to which lignin has been subjected.

RALPH L. HOSSFELD

School of Forestry  
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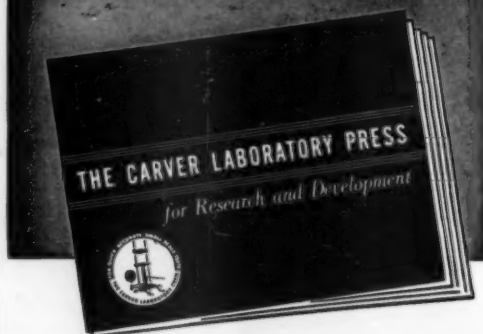
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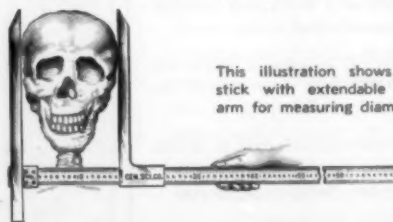
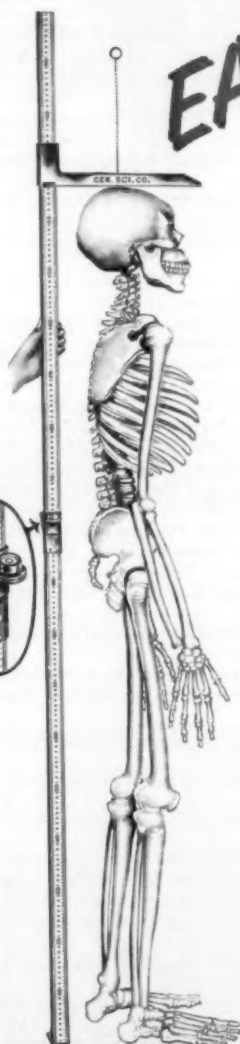
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- Aug. 8-15. International Geographical Union. Washington, D. C.
- Aug. 11-21. Union Radio-Scientifique Internationale. Sydney, Australia.
- Aug. 12-15. Poultry Science Association. University of Connecticut, Storrs.
- Aug. 12-16. Photographic Society of America (Annual). Hotel New Yorker, New York.
- Aug. 12-16. Plant Science Seminar (Annual). Philadelphia.
- Aug. 15-22. International Conference of Agricultural Economists. East Lansing, Mich.
- Aug. 17-23. American Pharmaceutical Association. Hotel Bellevue-Stratford, Philadelphia.
- Aug. 17-23. International Grassland Congress. Pennsylvania State College, State College.
- Aug. 18-22. Seminar in Industrial Instrumentation. Minneapolis-Honeywell Regulator Company, Philadelphia.
- Aug. 19-22. American Institute of Electrical Engineers (Pacific General). Hotel Westward Ho, Phoenix, Ariz.
- Aug. 20-27. Australian and New Zealand Association for the Advancement of Science (Annual). Sydney.
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- Aug. 25-29. Oak Ridge Summer Symposium on “The Role of Atomic Energy in Agricultural Research.” Oak Ridge, Tenn.
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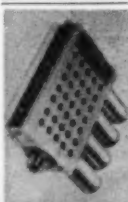
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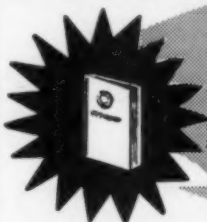
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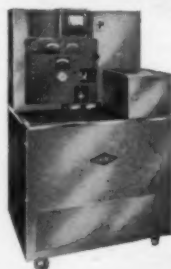
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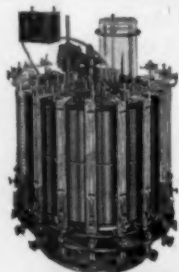


The large Aminco-Stern research model (left) is intended for heavy work output, using a large variety of sample volumes. The Aminco Portable Apparatus (right) is designed for routine research and clinical use on a smaller scale. Both models constitute complete electrophoresis laboratories in single, compact units. They combine precise schlieren optics, automatic refrigeration, high-voltage supply, and rapid dialysis facilities. Accessories available for macro-preparative work, adsorption chromatography, diffusion measurements, and routine clinical analysis.

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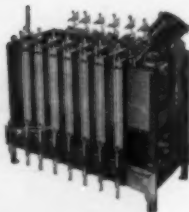


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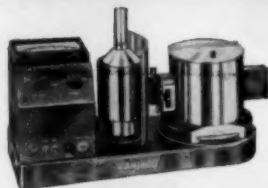


These greatly improved instruments represent the latest developments in manometric apparatus. The Aminco-Lardy Rotary Warburg Unit (left) can be rotated so that any manometer can be brought before the operator while he remains in a fixed position. Manometers may be read while in motion, or stopped individually. The Dual-shaker Apparatus (right) embodies two independent shaking mechanisms. Both types have wobble-free manometers, and are available in heated and refrigerated models.

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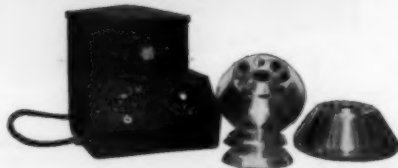
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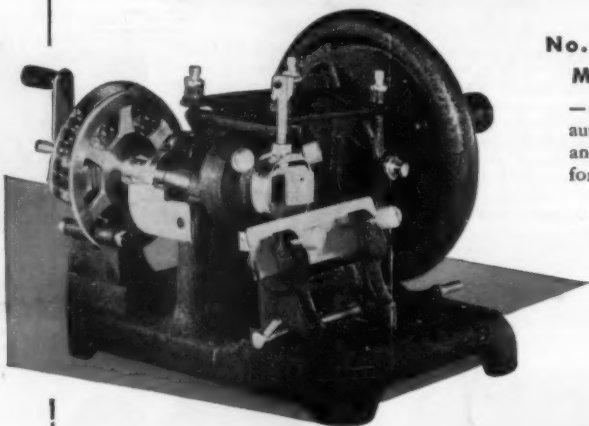
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